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# THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES

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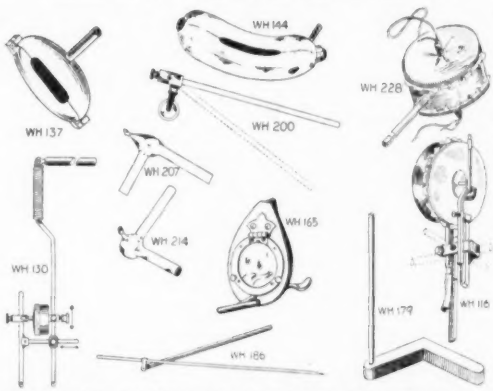


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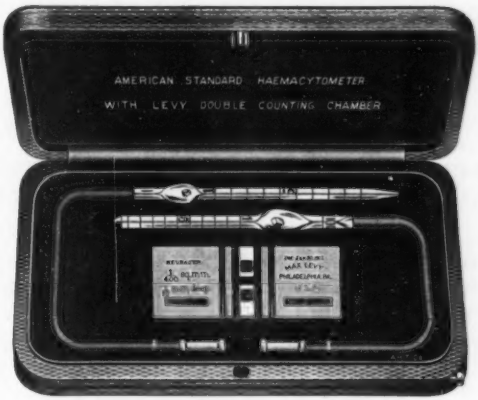


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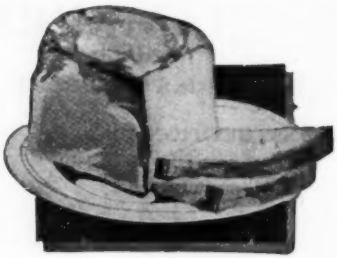

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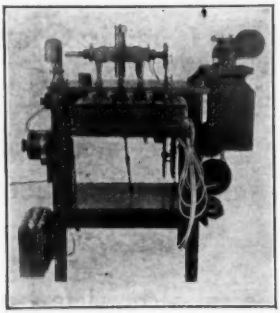

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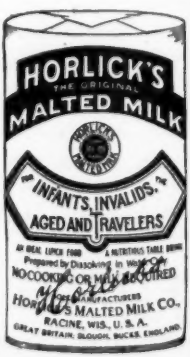

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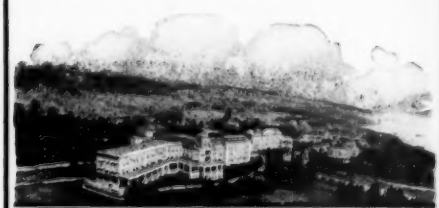

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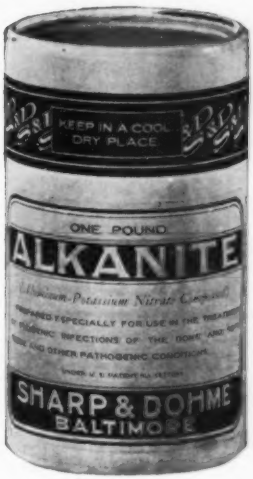

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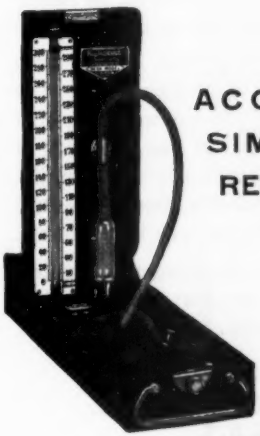

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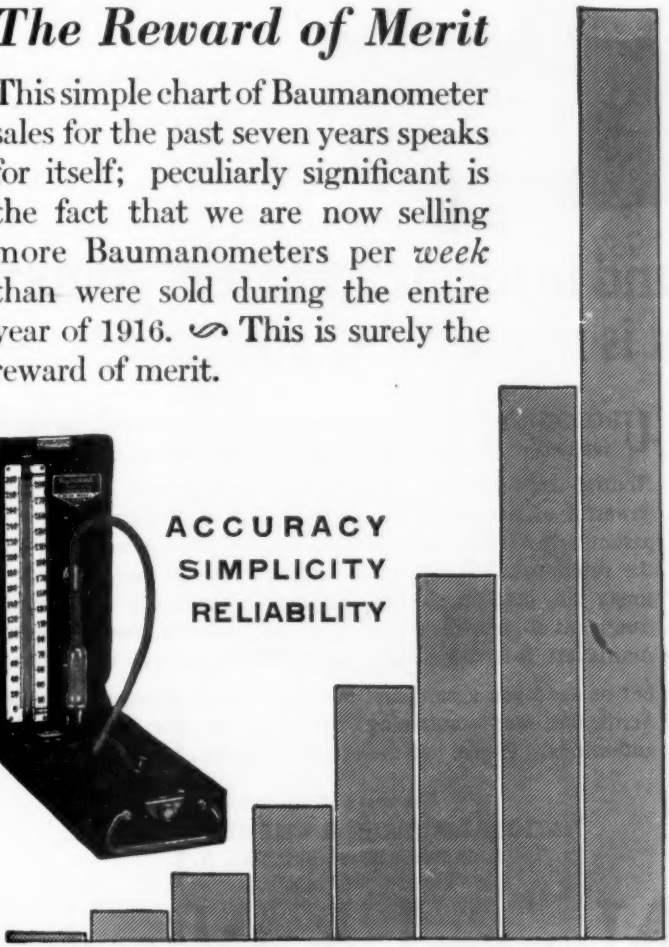


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## ORIGINAL ARTICLES.

# THE RETAINED GALL-BLADDER: ITS COMPLICATIONS, AND THE DIFFICULTIES AND DISADVANTAGES OF SECONDARY CHOLECYSTECTOMY.*

By De Witt Stetten, M.D.,

NEW YORK, N. Y.

While the trend of surgical opinion, until quite recently, has been that cholecystectomy is the operation of choice in the vast majority of cases of gall-bladder disease, the question is as yet by no means definitely settled. It is quite generally agreed that the gall-bladder should not be extirpated in any form of irremovable occlusion of the common duct. Most surgeons believe that cholecystectomy is somewhat more of a procedure than cholecystostomy and that, therefore, the latter operation should be performed, as an emergency measure, in very critical cases, especially in very severe, acute, fulminating infections, in cases where there are very extensive adhesions or other great technical difficulties, in late pregnancy, in the very aged, in much debilitated, undernourished or very fat patients, in advanced cardiac decompensation or pulmonary tuberculosis, in serious chronic bronchitis or emphysema, in extreme anemia, in hemophilia, in uncontrollable diabetes, in renal insufficiency, or in the presence of marked or protracted cholemia. It is a universal opinion that a gall-bladder which is seriously damaged or ulcerated, which is the seat of malignant disease, or whose cystic duct is obliterated should be removed. In all the other cases, which really comprise the great bulk of

* Read in part before the Binghamton, N. Y., Academy of Medicine, January 17, 1922.

gall-bladder operations, there is still considerable divergence of opinion, with the tendency just at present for the pendulum to swing backward toward retaining the gall-bladder unless that organ is hopelessly diseased. Much is now being written of the functions of the gall-bladder and its importance to the organism. The *Journal of the American Medical Association* of November 26, 1921, and February 25, 1922, discusses the subject editorially, as does, *Surgery, Gynecology and Obstetrics* in March, 1922. These editorials, which are based upon the most modern research on the subject, are frankly warnings to the surgeon not to consider the gall-bladder as a functionless organ. Other writers take quite the opposite view and regard the gall-bladder of almost as little importance to the organism as they do the appendix. One of the most recent contributions with this leaning is a very complete analysis of the subject, with full bibliography, by Harer, Hargis and Van Meter.[7] Their conclusions, aside from the belief that the gall-bladder acts as a concentrater of the bile by lymphatic absorption, almost agree with those of Woods Hutchinson[8] and others in considering the gall-bladder a vestigial structure. Two other very recent papers by Jacobson and Gydesen,[22] and by Auster and Crohn,[23] based upon experimental studies, have similar inclinations. The former see little use for the gall-bladder, except the minimizing of extremes of pressure in the biliary system, while the latter feel that the usual bile flow disregards the gall-bladder altogether, that the gall-bladder has no contractile function to speak of, that its outflow is in the nature of an overflow incontinence, but that, under pathological conditions, it may relieve intraductal pressure. Both papers refer to the concentration of the bile in the gall-bladder by dehydration, but both likewise indicate that its removal in the human being produces no definite, clinically demonstrable, deleterious effects.

Papers are still being published in which are discussed the indications and contraindications for cholecystectomy as against cholecystostomy. To be sure, the Mayo Clinic, whose dicta exert a marked influence on surgical thought in the United States, has come out strongly for cholecystectomy as the routine procedure—as demonstrated by the chapter on Gall-bladder Surgery in the latest volume of *Keen's Surgery* by William J. Mayo and Donald C. Balfour.[17] According to this article, there are no two sides to the question. This opinion from Rochester, however, is only a comparatively late development, having gradually come to the fore about nine years ago. As recently as 1908, William J. Mayo[15] expressed himself emphatically against the removal of the gall-bladder as the operation of choice, and only in 1914 did he,[16] by a very gradual and unostentatious transition, show that he was changing his mind. Since that time, the opinion of the Mayos, based upon their enormous material, has been quite consistently

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in favor of cholecystectomy. Yet it was not before 1916, in a symposium upon "Cholecystostomy *versus* Cholecystectomy," at the Clinical Congress of Surgeons of North America, that Charles H. Mayo[14] made a statement, clear-cut and crystallized, favoring the latter operation. At that same symposium, Lund[12] was, if anything, more emphatic than Mayo, while Deaver[2] had much more to say in favor of cholecystostomy than either of the other two. The opinion of Lund and the Mayos, however, is by no means universally accepted even in this country. The latest editions of such standard text-books as Binnie[1] and Ochsner (Ransohoffs[18]) still discuss the *pros* and *contras* of the subject at length, and articles are constantly appearing in the surgical literature condemning routine cholecystectomy and advocating conservation of the gall-bladder. So far as the European surgeons are concerned, there still seems to be considerable doubt in their minds. Kehr,[10, 11] in his most recent publications, before his death, staunchly advocated cholecystectomy, but his opinion is by no means generally shared by the other surgeons of Europe, particularly by our English colleagues.

The usual method of argumentation in favor of cholecystostomy as against cholecystectomy has been to emphasize the fact that the gall-bladder is an important organ with vital functions which are more or less clearly understood. It is contended that its routine removal involves serious dangers or disadvantages to the individual, such as dilatation of the bile ducts, relaxation of the sphincter of Oddi and subsequent ascending infection of the biliary passages, or digestive disturbances from dribbling of bile, so-called "biliary incontinence," while its retention is of great value and importance in storing and concentrating the bile, and in regulating its tension in the biliary system and its intermittent flow into the duodenum by "contrary" or "reciprocal" innervation. I believe that it might be worth while now to approach again the question from the reverse point of view, to analyze specifically the complications that may arise from retaining the gall-bladder and to study in detail the difficulties and disadvantages of a secondary removal of that organ. I have tried to base my deductions mainly upon personal observations in a series of cholecystostomized patients, who, either soon after the drainage of the gall-bladder, developed troublesome symptoms, or whose recurrence may have been postponed for periods varying from a few months to many years. The majority of these cases have later come to secondary cholecystectomy.

I shall first discuss:

**I. The Complications of the Retained Gall-bladder.** Although some of the cases have not come to secondary removal of the gall-bladder, even these show rather well-defined clinical pictures, so that they can be readily classified with the operative cases.

On the basis of the essential lesions found at operation, I have attempted to group the cases in the following manner:

1. Fistulæ. One of the most frequent complications of cholecystostomy is the formation of a persistent fistula. There are two distinct types of fistula—mucous and biliary—depending, as the names imply, upon whether the discharge is merely mucous secretion from the gall-bladder or a drainage of bile. Both types of fistulæ may be continuous. They are, however, usually intermittent in character, giving rise to pain in the gall-bladder region, frequently chills and fever, and, in the case of biliary fistulæ, distinct icterus, when they are closed. Immediate relief follows the spontaneous or artificial opening of the fistula and the discharge of the retained mucus or bile.

(*a*) *Mucous Fistulæ.* Mucous fistulæ following cholecystostomy are invariably due to occlusion of the cystic duct of the retained gall-bladder, the discharge being the secretion of its mucous membrane.

This occlusion may be due either to a complete inflammatory or cicatricial stricturing of the cystic duct, or to a retained calculus, impacted in the duct itself or in the neck of the gall-bladder, or to both. The mucous fistula may develop immediately after cholecystostomy or there may be a period of biliary drainage. Then, as the cystic duct becomes more or less occluded by stricture or by impaction of a calculus, only mucus is discharged. The stricture may open or the calculus may move and the fistula may then discharge bile for a time and close. If the stricture closes or the calculus becomes impacted again, the mucous fistula may reform before or after the external wound has closed. This intermittent mucous-biliary fistula is not an uncommon variety. Should conditions favor it (see under Biliary Fistulæ), after the cystic duct occlusion has been overcome, a mucous fistula may become converted into a persistent biliary fistula. Let me mention a few examples of mucous fistula:

Case I.—(Office.) Female, aged eighty-four years. Twenty-three years ago she was operated upon for gall-stones. Numerous calculi were removed and the gall-bladder was drained. The wound has never closed. The discharge has always been mucous. Owing to the patient's advanced age, operation is, of course, not to be considered. The cystic duct must be occluded—probably obliterated by cicatrization (Fig. 1).

Case II.—(Office.) Female, aged thirty-three years. In 1916, she had been operated upon for gall-stones with drainage of the gall-bladder. Bile drained for a short time and then a mucous fistula developed which refused to close permanently. When the secretion ceased, the patient ran high temperatures, and suffered

from severe pain in her gall-bladder region. I advised cholecystectomy, which was done in her home city a year after her first operation. A strictured cystic duct was found (Fig. 1). The patient has been perfectly well since.

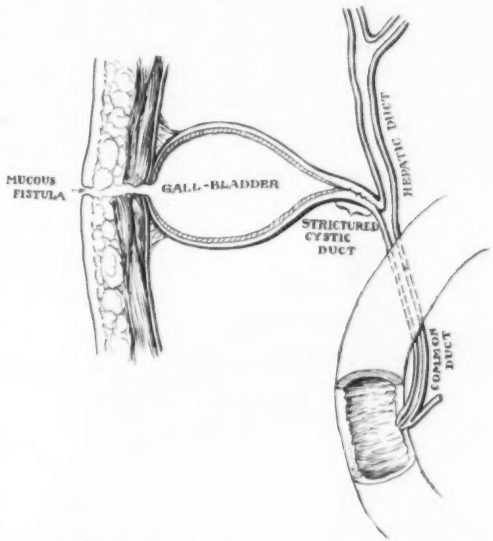


FIG. 1.—Cases I and II. Mucous fistula, due to total stricture of cystic duct.

CASE III.—(No. P. 1334, 1919.) Male, aged fifty-two years. On March 18, 1918, he was operated upon for an acute empyema of the gall-bladder. No stones were recovered and the gall-bladder was drained. The wound did not close. There was an alternating mucous and biliary fistula. I performed a cholecystectomy on March 28, 1919, twelve months after his first operation, and removed a shrunken and thickened gall-bladder, very adherent to the anterior abdominal wall with a calculus in the cystic duct, not absolutely impacted, but quite snug (Fig. 2). Prompt healing followed.

CASE IV.—(Nos. P. 2385, 1920, and 3030, 1920.) Female, aged sixty-four years. I first saw her in April, 1918, after she had been operated upon for an acute empyema of the gall-bladder some months previously. In addition to a large ventral hernia through the wound there was a mucous, and at times a mucous-biliary fistula. This fistula occasionally closed and when it did there was a rise of temperature and pain in the gall-bladder region. Owing to the patient's poor general condition, I advised temporizing and

the fistula finally seemed to heal without untoward symptoms. On August 18, 1920, she developed an acute intestinal obstruction, due to a band in the gall-bladder region tying off a loop of ileum. I released the band, separated numerous intestinal adhesions and repaired the hernia. She made a satisfactory recovery and remained well until November 22, 1920, when she developed an acute abscess in the old gall-bladder which broke through into the abdominal wall. The pus was slightly bile-stained. A cholecystectomy revealed a contracted gall-bladder with a calculus in the cystic duct, rather tightly impacted (Fig. 2). To the gall-bladder, and under the surface of the liver, the duodenum and hepatic flexure of the colon were densely adherent (Fig. 18).

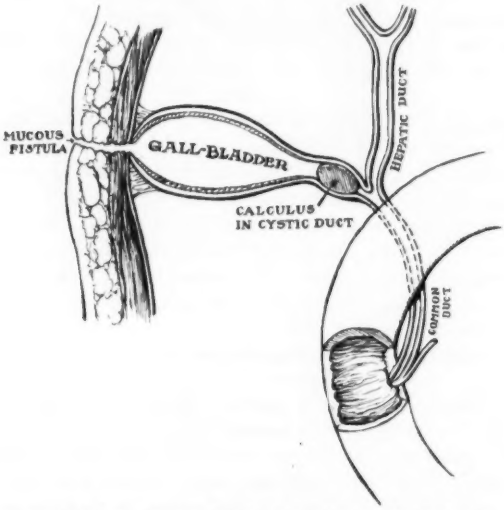


FIG. 2.—Cases III and IV. Mucous fistula, due to impacted calculus in cystic duct. Shrunken gall-bladder.

In the two previous cases, of course, the calculus in the cystic duct was overlooked at the first operation. Had a cholecystectomy been done this oversight would not have occurred. The cystic duct stone would have been removed with the gall-bladder.

The following case illustrates how the retention of an impacted calculus in the neck of the gall-bladder, combined with a total stricture of the cystic duct, served to produce a mucous fistula, which would have been avoided by primary cholecystectomy:

CASE V.—(No. P. 3150, 1922.) Female, aged thirty-one years. This was a patient of Dr. Hermann Fischer's, who, four months previously had been operated upon for some acute gall-bladder

disease accompanied with high fever and slight jaundice. The gall-bladder was drained and the patient does not know whether or not any stones were removed. The fistula never healed. At first it drained pure bile, but later only a slightly yellowish-colored mucus. She also complained of pain in the region of the fistula and fullness and soreness in the epigastrium after eating. She was operated upon, November 20, 1923, by Dr. Fischer, who excised the fistula and with much difficulty and hemorrhage, isolated and removed the gall-bladder which was imbedded in a mass of adhesions including the liver, stomach, duodenum and hepatic

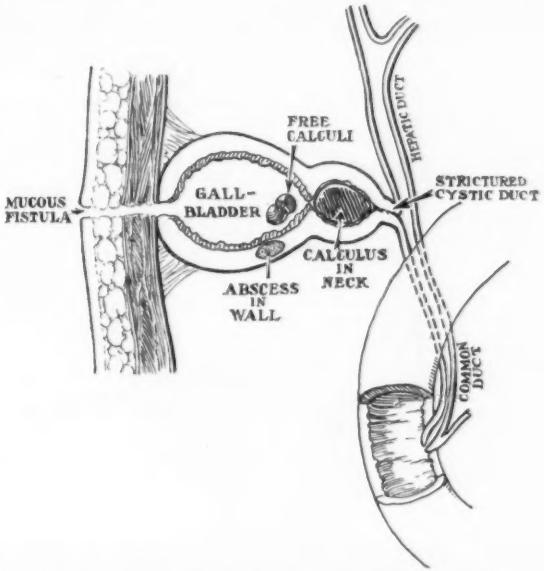


FIG. 3.—Case V. Mucous fistula, due to both impacted calculus in neck of gall-bladder and to total stricture of cystic duct. Thickened gall-bladder with two additional free calculi in lumen and small chronic abscess in wall.

flexure of the colon. The gall-bladder was a thickened, somewhat contracted organ. In the main cavity were two small calculi and lodged in the neck, which was separated from the main cavity by an hour-glass contracture, was a large ovoid calculus. The cystic duct was completely strictured and in the wall of the gall-bladder was a small chronic abscess (Fig. 3). The convalescence was uneventful.

(*b*) *Biliary Fistulæ.* Biliary fistulæ are due to a variety of causes. In some instances the biliary fistula is not due to the retained gall-bladder, *per se*, but to an incomplete operation and

the leaving of calculi in the common duct. In a measure, the neglect to dissect out the gall-bladder and expose the ducts to proper inspection and palpation is responsible for even this complication. Let me illustrate:

Case VI.—(No. 1716, 1912.) Male, aged thirty-seven years. In February, 1912, he was operated upon for gall-stones. Several fair-sized calculi were removed from the gall-bladder and the gall-bladder was drained. A continuous biliary fistula developed and reoperation by me on April 15, 1912, about two months after his first operation, disclosed the fact that a large stone in the common duct, impacted at the papilla, had been overlooked.

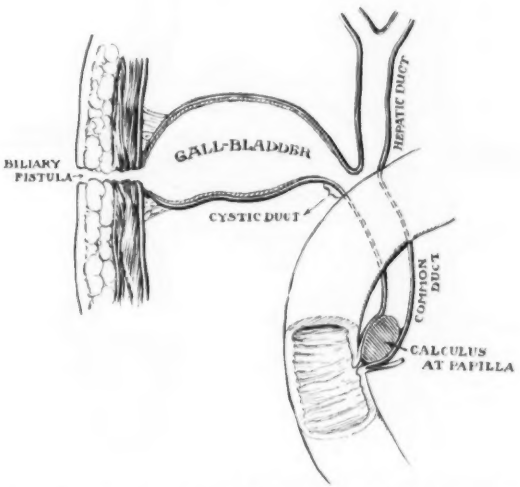


Fig. 4.—Case VI. Biliary fistula, due to impacted calculus in common duct at papilla. Hepatic and common ducts somewhat dilated.

The thickened gall-bladder was imbedded in adhesions, and the hepatic and common ducts were somewhat dilated. He was cured by choledochotomy, extraction of the calculus, cholecystectomy and hepatic drainage (Fig. 4). Microscopical examination of the gall-bladder showed a chronic cholecystitis.

Case VII.—(No. 862, 1917.) Female, aged sixty-one years. In 1915, she had been operated upon for gall-stones with jaundice. One large, solitary calculus was removed from the gall-bladder and drainage instituted. When the drainage of bile ceased, she developed very severe pain in the gall-bladder region and one year after her first operation a cholecystectomy was performed by another surgeon. She then developed a biliary fistula, which was

almost continuous, except for an occasional stop. During the stoppage there was pain and fever. On February 12, 1917, eight months after her second operation, I excised the fistulous tract, removed two moderately large stones from the dilated common duct and drained the biliary system (Fig. 5). The fistula closed promptly.

A second very common form of biliary fistula after cholecystostomy is that due to the formation of a so-called "lip" or mucocutaneous fistula, where the mucous membrane of the gall-bladder, adherent to the abdominal wall, becomes continuous with the epithelium of the skin. This cannot heal any more than a fecal fistula of the same character. Typical cases of this nature are the following:

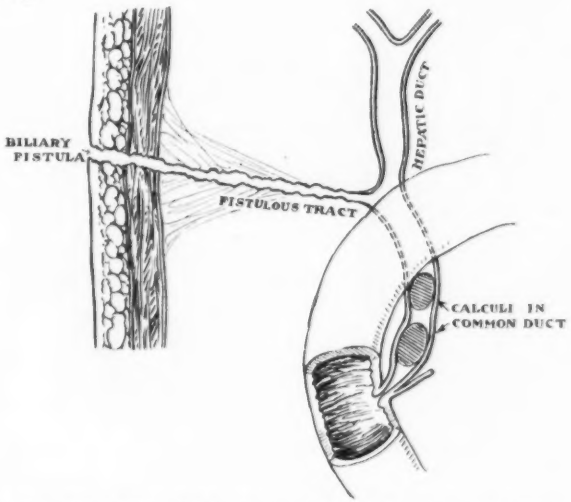


FIG. 5.—Case VII. Biliary fistula after secondary cholecystectomy, due to retained calculi in dilated common duct.

CASE VIII.—(Private.) Male, aged thirty-six years. On August 3, 1905, a cholecystostomy was done for a severe, septic empyema of the gall-bladder, and a very large calculus, practically the cast of the gall-bladder, was extracted. I assisted Dr. Frederic Kammerer at this operation and later had the after-care of the patient. A total biliary fistula developed, due to the growth of the mucous membrane to the skin (Fig. 6). The "cork experiment" showed that the common duct was patent, and following the teachings of a time when cholecystectomy was not as popular as it is today, on October 26, 1905, nearly three months after the primary operation, Dr. Kammerer successfully closed the fistula by loosening the mucous membrane from the skin and

suturing the gall-bladder, much as we close a fecal fistula at the present time.

Case IX.—(No. 2892, 1913.) Male, aged forty years. Two months previously the gall-bladder had been drained and several calculi removed. The biliary fistula refused to close on account of the proximity of the mucous membrane of the gall-bladder to the skin (Fig. 6). Some bile flowed into the intestine. On June 18, 1913, I separated the fistulous opening from the abdominal wall and succeeded in closing it by purse-string inverting sutures. Today I would unhesitatingly perform a cholecystectomy in a similar case.

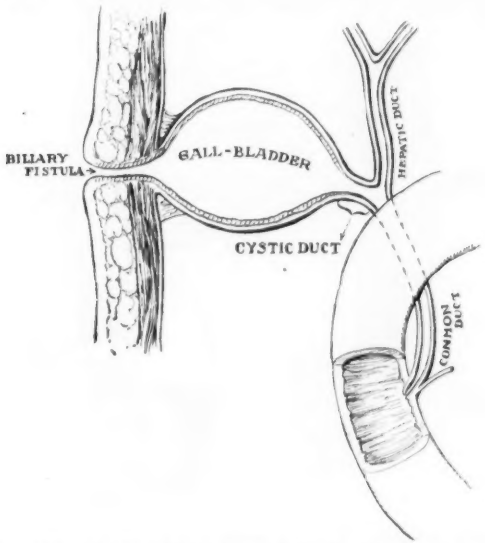


Fig. 6.—Cases VIII and IX. Biliary fistula, due to formation of mucocutaneous fistula.

A third variety of biliary fistula is due to a kinking or angulation of the junction of the hepatic and common ducts, because of the pull of the gall-bladder which is attached to the abdominal wall, and which, after drainage, frequently shrinks decidedly. I published such a case in 1913.[19]

Case X.—(No. 3693, 1912.) Female, aged nineteen years. I performed a cholecystostomy on July 24, 1912, and removed five medium-sized stones. Drainage was carried out in the usual manner. Bile drained freely at first, but then ceased. Severe pain and icterus developed, and the gall-bladder wound was reopened, with resulting profuse biliary drainage. This drainage

of bile continued for nearly a month, and on August 17, 1912, I reoperated. I found a much changed and contracted gall-bladder, adherent to the anterior abdominal wall, with a kink at the junction of the hepatic and common ducts, evidently due to the pull of the gall-bladder (Fig. 7). The angulation at the junction of these ducts was less than 45 degrees, and an actual valve-like formation prevented the bile flowing from the liver in its normal direction. There were no further calculi in the gall-bladder or ducts. The hepatic duct was markedly dilated, and the common duct narrowed, but when the gall-bladder was loosened and removed, and the common duct opened, a large probe was easily inserted into

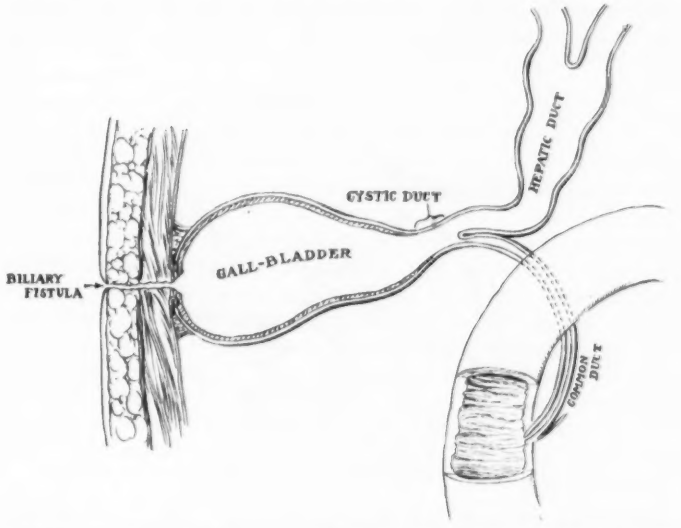


FIG. 7.—Case X. Biliary fistula, due to angulation of junction of hepatic and common ducts. Marked dilatation of hepatic duct, narrowing of common duct and valve-like formation at junction.

the duodenum through the papilla. The fistula closed promptly after cholecystectomy and the resultant straightening of the hepatic and common ducts.

Another case that might be mentioned in this group, although there was no actual fistula but rather the symptoms of common duct obstruction due to a marked contraction of the gall-bladder after cholecystostomy, is the following:

CASE XI.—(No. 2739, 1908.) Female, aged thirty-three years. She had been operated upon three weeks previously, July 20, 1908,

by another surgeon. Stones had been removed and a cholecystostomy performed. The bile drainage ceased promptly and the wound began to close when the patient became jaundiced and severe, cramp-like pains in the gall-bladder region developed. It was assumed that a stone in the common duct had been overlooked, and on August 10, 1908, I attempted to reopen the gall-bladder to establish drainage. With great care I tried to expose the gall-bladder and what seemed to be that organ, firmly adherent to the anterior abdominal wall, was finally exposed and opened. Bile escaped and a tube was inserted for drainage. The drained organ proved to be the duodenum (Fig. 17), and a duodenal fistula developed which unfortunately resulted in the death of the patient from inanition, in spite of all efforts at closure, including gastroenterostomy and pyloric exclusion. Postmortem examination

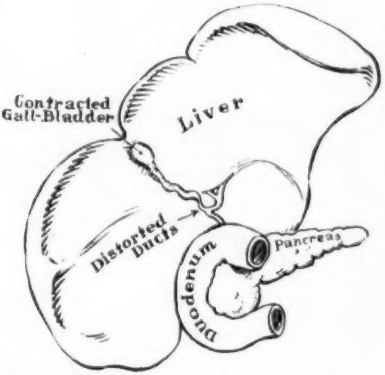


FIG. 8.—Case XI. Shrunken gall-bladder with distortion of ducts.

revealed an extremely shrunken gall-bladder continuous with the old sinus tract and some distortion of the ducts due to the pull of the shrunken organ (Fig. 8). There were no calculi in the gall-bladder or ducts and the ducts were patent.

It should here be noted that, in certain instances, a cholecystostomy wound will close more or less permanently, even if the cystic or common duct is obstructed by stricture, distortion or the retention of a calculus, provided the obstruction is only partial at the time. If, however, the occlusion becomes more complete or infection supervenes, the clinical picture of hydrops or empyema of the gall-bladder, common duct obstruction or cholangitis will, of course, develop just as in cases that have not been previously operated upon.

2. RETENTION OR REFORMATION OF CALCULI WITH ATTENDANT LESIONS. In addition to those cases cited under the previous

heading, in which calculi in the cystic or common duct had been overlooked, in a measure because primary cholecystectomy was not done, and where a mucous or biliary fistula formed, there are other cases of cholecystostomy in which calculi are inadvertently left free in the gall-bladder. In these latter cases the operative wound closes, but symptoms of biliary colic recur, with or without signs of acute infection or jaundice, often very promptly after operation, as, for example:

Case XII.—(No. P. 1266, 1915.) Female, aged fifty-six years. Twenty-two years ago she was operated upon for gall-stones. A number of stones were removed and the gall-bladder was drained. Four and a half weeks after the operation she had a typical attack of biliary colic and claims that calculi were found in the stool. Since then she has had more than a dozen attacks of rather severe, gall-stone colic, followed, usually, by jaundice. For the past few years the attacks have been somewhat less frequent and less severe and she prefers to postpone radical measures.

In other cases it is probable that calculi have reformed in the retained gall-bladder. Of course, it is well-known that gall-stones may form in the common and hepatic ducts and even in the liver, but the chance of reformation is greatly increased by the retention of the gall-bladder, because this organ is the principal seat of the process. To be sure, one can never be certain that the so-called cases of recurrence are really instances of recurrence at all. They may be the result of incomplete operation and non-removal of all the stones present at the time of the original operation, as in the case just described. I have, however, met with certain cases that seem to be *bona fide* recurrences. With the recurrence of the calculi, any sequel may develop, as with the primary stones, as, for instance, in the cases mentioned below, namely empyema of the gall-bladder, common duct obstruction, or chronic cholecystitis with lodging of the calculus in the cystic duct.

Case XIII.—(No. 307, 1921.) Male, aged forty years. Eight years ago he had been operated upon for gall-stones. Several stones had been removed and a cholecystostomy had been done. The drainage sinus closed within a normal period, and the patient remained well for about three years. He then had repeated attacks referable to the gall-bladder, finally culminating in a very acute condition. On January 18, 1921, I operated upon him for an acute empyema of the gall-bladder. I found and removed a very large, very thick-walled and inflamed gall-bladder adherent to the anterior abdominal wall and distended with seropus. The mucosa was gangrenous. Free in the gall-bladder were two calculi, the size of hazel-nuts (Fig. 9). The cystic duct was completely stenosed. The patient made an uneventful recovery. The original operation had been performed by a very competent surgeon, and it is incon-

ceivable that these two large stones could have been overlooked if they had been in the gall-bladder at the time, nor could they have been left in the ducts and later have entered the gall-bladder, because the wound healed promptly after the first operation.

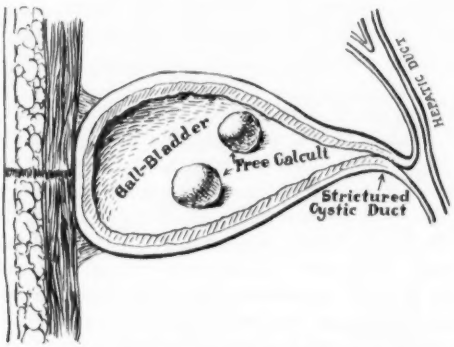


FIG. 9.—Case XIII. Thickened and distended gall-bladder with recurrent calculi. Total stricture of cystic duct.

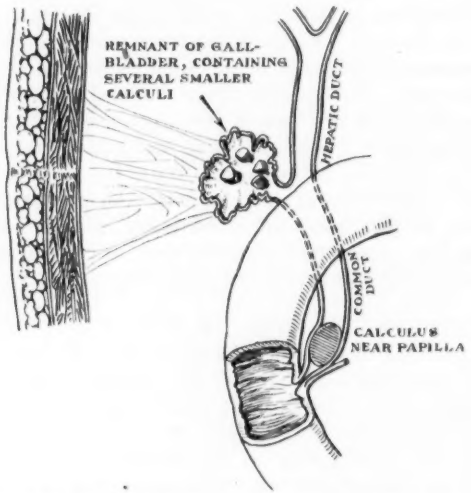


FIG. 10.—Case XIV. Recurrent calculi in remnant of gall-bladder and dilated common duct.

CASE XIV.—(No. P. 3282, 1920.) Female, aged sixty-seven years. In 1912, she had been operated upon for gangrene of the gall-bladder. A large number of gall-stones had been removed

and likewise a portion of the gall-bladder. At the time of the operation there was no evidence of calculi in the ducts. She was well until a little over a year ago when she developed symptoms that pointed to an intermittent common duct obstruction. She had had three or four attacks of pain resembling biliary colic, followed by jaundice. At operation, December 18, 1920, I found the remnant of the gall-bladder imbedded in adhesions. The gall-bladder stump contained several smaller stones, and in the dilated common duct was a large stone near the papilla (Fig. 10). She was cured by choledochotomy, extraction of the common duct stone, the removal of the remains of the gall-bladder and its contents and hepatic drainage. In this case it is possible that the presence of the calculi was the result of an incomplete operation, although the operating surgeon claimed that there was no recognizable evidence, at the time, of any remaining stones either in the gall-bladder remnant or in the ducts. Further, if these stones had not reformed since the operation, it is almost inconceivable why the patient should have remained well for over seven years.

Case XV.—(No. P. 403, 1922.) Female, aged forty-one years. A large solitary gall-stone was removed and the gall-bladder drained in 1916. For four years she was in moderately good health, but two years ago she began to suffer from pain, sometimes diffused, sometimes localized in the right hypochondrium where there was definite sensitiveness to the touch. There was a diarrheal tendency. Operation on February 22, 1922, disclosed an infiltrated, friable gall-bladder, imbedded in omental adhesions and adherent to the duodenum. In the cystic duct was a typical solitary, nonfacetted, cholesterin calculus, the size and shape of an olive (Fig. 11). The patient was entirely freed of her symptoms by cholecystectomy. The gall-bladder showed the usual changes of a chronic cholecystitis.

In this case the character of the stone is almost conclusive evidence of its being a definite example of reformation. The relative freedom from symptoms for four years after the first operation and the recurrence of her illness two years ago corroborates this inference.

3. Adhesions. There is a group of cases after cholecystostomy where the patients are not cured and where the symptoms seem to be due essentially to adhesions between the abdominal wall and the retained gall-bladder. When one realizes that adhesions, merely of the omentum to the anterior abdominal wall, following an appendectomy or a gynecological laparotomy, are often the source of such disturbances that relaparotomy becomes necessary to loosen these adhesions, as I have observed in quite a series of

cases, it is understandable that a gall-bladder, with the adjacent liver edge, that becomes tightly plastered to the abdominal scar can cause sufficiently annoying symptoms, either directly or reflexly, to make its victim a real invalid. Frequently, these adhesions also include the duodenum and pyloric portion of the stomach and, often, even the hepatic flexure of the colon. The following are my observations where I believe the adhesions, *per se*, were, in the main, responsible for the continued illness of the patient:

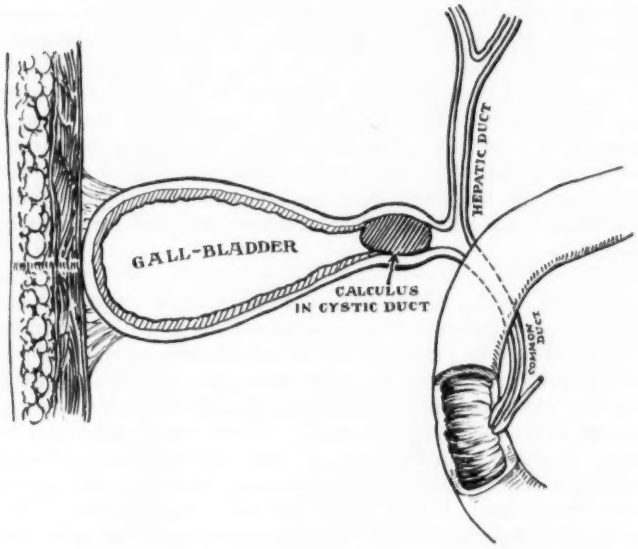


FIG. 11.—Case XV. Large solitary recurrent calculus impacted in cystic duct. Somewhat thickened gall-bladder adherent to anterior abdominal wall.

CASE XVI.—(U. S. Army Embarkation Hospital No. 4.) Female, aged thirty-six years. In 1916, she had been cholecystostomized for multiple calculi. She was never well after the operation, but suffered continuously from annoying pains in the gall-bladder region, particularly on standing and bodily exertion. As she was a nurse, this handicapped her considerably and, finally, in April, 1919, three years after her first operation, I did a cholecystectomy. I found a rather elongated gall-bladder, very densely adherent to the anterior abdominal wall, in such a way that the edge of the liver was actually turned back upon itself. Adhesions between the liver edge and the anterior abdominal wall were also present (Fig. 12). After the loosening of all adhesions and the removal of the gall-bladder, the patient was entirely freed of her symptoms.

CASE XVII.—(No. 3475, 1921.) Female, aged thirty-nine years. About five years ago the gall-bladder had been drained for a cholecystitis without stones. There was more or less continuous pain in the gall-bladder region following the operation. On June 20, 1921, I operated upon this patient and found the gall-bladder imbedded in omental adhesions and adherent to the anterior abdominal wall at the costal border. The adhesions were separated and the gall-bladder removed. Microscopical examination of the gall-bladder showed a chronic cholecystitis. Her pain ceased after the operation.

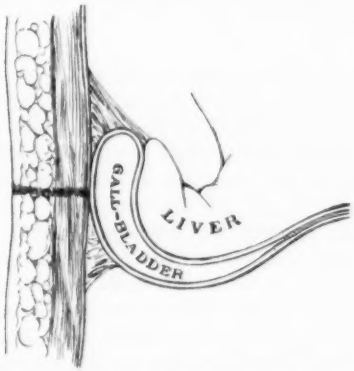


FIG. 12.—Case XVI. Elongated gall-bladder densely adherent to anterior abdominal wall and turning liver edge back upon itself.

CASE XVIII.—(No. 3229, 1921.) Male, aged twenty-two years. Two and a half years ago he had been operated upon for some gall-bladder trouble. The gall-badder had been drained, although no stones were found. The patient remained quite well for a year and nine months, when he began to vomit after every meal and suffered from cramp-like abdominal pains. The bowels moved freely, even with a diarrheal tendency. This vomiting continued for three months, and became so severe at the end of that time that the patient came to the hospital in an extremely weakened condition. He was so ill that rectal feeding was necessary. The roentgen-ray examination was not conclusive, but suggested adhesions of the pylorus and duodenum to the gall-badder region. An exploratory laparotomy by me on June 1, 1921, revealed a gall-bladder adherent to the anterior abdominal wall and imbedded in dense adhesions, and adhesions of the pylorus and duodenum to the gall-bladder. The adhesions were separated, the gall-bladder removed and the patient made an uneventful recovery.

Case XIX.—(No. 1652, 1922.) Male, aged thirty-eight years. In 1919, his gall-bladder was drained for what was supposed to be a cholecystitis without stones. For some years, he has been a sufferer from marked gastric symptoms which the roentgen-ray showed to be due to a deep, penetrating ulcer of the lesser curvature. On March 22, 1922, I performed a partial gastric resection with gastroenterostomy. The operation was much complicated and protracted by the adhesions between the gall-bladder, anterior abdominal wall, omentum and duodenum. The isolation of the duodenum was accomplished only with the greatest of difficulty. His stomach symptoms have been relieved, but he still has pain in the gall-bladder region and a secondary cholecystectomy is now being considered.

4. Recurrent Cholecystitis. The cases in this group merge more or less with those in the group discussed just previously. In Case XVII, for instance, the gall-bladder was much thickened and microscopical examination showed a chronic cholecystitis. It is possible that some of the symptoms were due to this chronic inflammatory condition. It is difficult to separate the cases in which the symptoms are due purely to adhesions, and those in which the symptoms are due to a recurrence of an inflammatory lesion in the gall-bladder. In most cases, both lesions are probably responsible for lack of cure. The cholecystitis may be either in the form of recurring acute or subacute attacks or may be more of a chronic affair. The following are illustrations of where the cholecystitis, apparently, was the predominating factor in the illness of the patient:

Case XX.—(No. P. 2286, 1908.) Female, aged thirty-five years. On June 17, 1908, I performed a typical cholecystostomy for a severe, acute empyema of the gall-bladder, which contained numerous small stones. The wound healed very slowly—a fistula, first biliary, then mucous, remaining for months. About one year later she had a typical attack of acute cholecystitis, with a temperature of 104° F., slight icterus and an exquisitely sensitive gall-bladder region. This attack subsided and the patient remained fairly well for over ten years. In 1920, she had a number of moderately severe attacks, which were clearly referable to the gall-bladder, and I advised a secondary cholecystectomy. She has not yet consented to have this done, and manages to get along fairly well between attacks.

Case XXI.—(No. P. 2862, 1921.) Male, aged sixty-seven years. In 1901, he had a cholecystostomy performed. Numerous stones were removed from the gall-bladder and the patient made a satisfactory recovery. In the past three or four years this patient

has had several attacks of decided discomfort in the gall-bladder region. There is some sensitiveness to pressure and coincident digestive disturbance, referable particularly to the intestines. During the attack there is diarrhea and flatulence, presumably due to an enterocolitis, secondary to an exacerbation of infectious processes in the gall-bladder.

CASE XXII.—(Office.) Female, aged twenty-seven years. Two years ago several gall-stones were removed and cholecystostomy performed. She has recently consulted me, complaining of constant indigestion and pain in the right upper abdomen. The gall-bladder region is sensitive to pressure. Cholecystectomy for recurrent cholecystitis with adhesions has been advised.

CASE XXIII.—(Office.) Female, aged sixty-two years. Very recently I was consulted by this patient, who had been operated upon fifteen years ago. A very large gall-bladder containing over a hundred calculi was found. The stones were removed and the gall-bladder drained. She has never been well since the operation. She suffers from continuous pain in the right hypochondrium. At times this pain increases in severity and then she has attacks of nausea and vomiting. During these attacks there is a moderate rise of temperature. The gall-bladder region is markedly sensitive to pressure. Her trouble is undoubtedly due to a recurrent cholecystitis associated with adhesions between the gall-bladder and anterior abdominal wall. I have advised her to have her gall-bladder removed, and I believe that, sooner or later, she will be forced to follow my advice.

CASE XXIV.—(Office.) Female, aged twenty-four years. A little over a year ago she was operated upon for numerous very fine biliary calculi, which were removed, and the gall-bladder was drained. Five months after operation she had a very severe attack of pain in the gall-bladder region, probably due to a subacute cholecystitis. Since that time she suffers more or less continually with pain in her back and right hypochondrium, in all likelihood, the result of adhesions and chronic cholecystitis. Her appetite and digestion are poor. She is very sensitive to pressure in the gall-bladder region. I have advised cholecystectomy, and she is considering having the operation performed in the near future.

CASE XXV.—(Office.) Female, aged forty-three years. After an illness of five years, she was operated upon six years ago. A cholecystostomy was done and many small stones were removed. Recently, she has had attacks of discomfort in the gall-bladder region, with indigestion. There is distinct sensitiveness to pressure in the right hypochondrium. A diagnosis of recurrent chole-

cystitis with adhesions has been made and cholecystectomy has been advised.

CASE XXVI.—(Nos. P. 3339, 1913, and P. 790, 1921.) Female, aged thirty-eight years. On July 1, 1913, because of symptoms very definitely suggesting gall-stones, I operated and found a gall-bladder rather normal in appearance and loosely adherent to the duodenum. There were no calculi to be felt either in the gall-bladder or ducts. Adhesions were loosened and the gall-bladder retained. On March 21, 1921, because of persistent attacks of colicky pain in the gall-bladder region, I reoperated. Dense adhesions were found between the omentum, anterior abdominal wall, liver and gall-bladder and between the duodenum and gall-bladder. These adhesions were loosened and a rather thickened gall-bladder was found. Cholecystectomy was done. The cystic

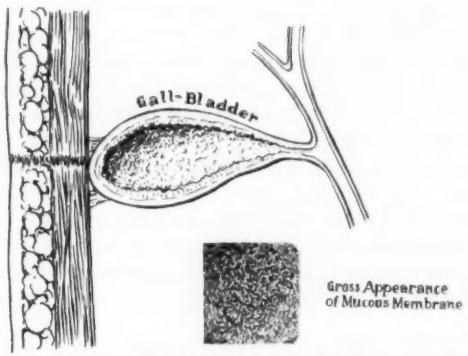


FIG. 13.—Case XXVI. Chronic cholecystitis. Insert shows gross appearance of papillary condition of mucous membrane.

duct was very friable and was ligated with difficulty. The gall-bladder showed a thickened wall with a mucosa studded with papillary excrescences (Fig. 13). Microscopical examination showed that the changes in the gall-bladder were purely of a chronic inflammatory nature. Of course, in this case the gall-bladder had not been drained. It was, however, an example of that condition, now so well recognized, namely, chronic cholecystitis without stones, where the gall-bladder should have been removed in the first instance. It is included in this paper because it is my conviction that even if the gall-bladder had been drained at the first operation, a secondary cholecystectomy would have been necessary. The patient has had no attacks since the removal of her gall-bladder.

A case somewhat similar to the preceding, but which has not yet come to reoperation, follows:

Case XXVII.—(No. P. 3432, 1922.) Female, aged thirty-four years. Since 1903, after an attack of typhoid fever, patient has suffered from severe attacks of pain in the right upper abdomen with vomiting. She was not relieved by an appendectomy in 1910, and six months later the gall-bladder was examined but, as no calculi were found, it was not removed and merely some adhesions were loosened. In 1914, an ileocolostomy was done because of very dense adhesions at and kinking of the hepatic flexure of the colon. Her symptoms were not relieved, and she is now a chronic invalid. Upon examination, there is definite sensitiveness in the right hypochondrium. While it is possible that some of her trouble is due to adhesions and the presence of the unilaterally excluded loop of cecum, ascending and part of the transverse colon, there is little doubt that much of her trouble is the result of recurrent attacks of cholecystitis and secondary adhesions. A cholecystectomy with possibly a resection of the excluded loop of colon, in one or two stages, has been advised and is now under consideration by the patient.

The following is an example of recurrent cholecystitis in the retained gall-bladder, culminating in a true empyema:

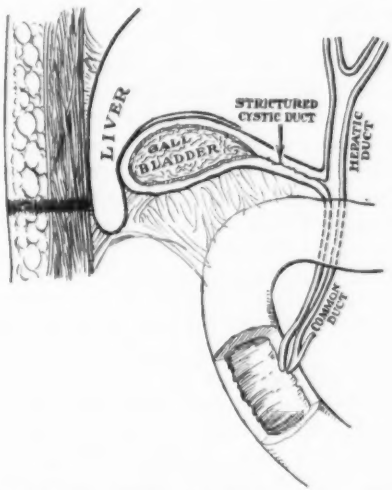


Fig. 14.—Case XXVIII. Shrunken gall-bladder filled with thick pus, with total stricture of cystic duct. Gall-bladder imbedded in adhesions, with adhesions of liver to anterior abdominal wall and of duodenum to liver and gall-bladder.

Case XXVIII.—(No. P. 8684, 1922.) Male, aged fifty years. Six years ago he had been operated upon for gall-stones, but the gall-bladder had not been removed. During the past six months, the patient has had three other severe attacks of pain in the right

upper abdomen, radiating to the back. He was seen by me suffering from what appeared to be an acute inflammation in the gall-bladder region, with a temperature of 103° F., complicated by a postoperative ventral hernia. Operation, on December 15, 1922, disclosed a thickened, shrunken gall-bladder, deeply imbedded in the liver and surrounded by a mass of adhesions of omentum, pylorus, duodenum, hepatic flexure of the colon and liver to each other and to the anterior abdominal wall. Cholecystectomy was performed with considerable difficulty, and hemorrhage, after the separation of the adhesions, and the hernia was repaired. The gall-bladder was a much diseased organ, and was filled with thick, yellowish pus, containing some calculous gravel. The cystic duct was obliterated, and the mucous membrane of the gall-bladder was largely destroyed (Fig. 14). Microscopical examination showed an acute suppurative inflammation with a necrosis of the mucosa and submucosa extending in places into the muscularis. An uneventful convalescence ensued. It is a curious coincidence that this patient is the brother of Case XIII, operated upon by me nearly two years previously, with almost an identical clinical history and surgical findings.

The next case strongly suggests a similar condition as in the one previously described, although it has not yet been reoperated upon:

Case XXIX.—(No. 2571, 1923.) Female, aged seventy-six years. On April 6, 1911, she was operated upon for an empyema of the gall-bladder. Two large calculi were removed and the gall-bladder was drained. A biliary fistula persisted for about four months but finally healed. In 1913, an abscess in the old scar was reopened and again bile drained for ten weeks. Since then she has had occasional mild attacks of pain and discomfort in the right hypochondrium. On April 2, 1923, she had an attack of severe pain in the epigastrium, radiating to the right shoulder, with vomiting, temperature of 103° F. and followed by slight jaundice. There is some sensitiveness over the old scar in the gall-bladder region. The roentgen-ray examination shows an unusually marked dilatation of the duodenum, probably indicative of a chronic duodenal obstruction due to adhesions. The attack is subsiding, but it was obviously an acute cholecystitis with either retained or reformed calculi in the gall-bladder or cystic duct. On account of the patient's age, the advisability of reoperation is still under consideration.

Let me here say a word upon the subject of typhoid infections of the gall-bladder. As is well known, it has been quite definitely shown that the gall-bladder is the chief breeding place of the typhoid bacillus in typhoid carriers. Hence, even more so than in the ordinary catarrhal or suppurative inflammations of this organ, in acute, subacute or chronic typhoid cholecystitis or in

simple typhoid carriers without decided inflammatory changes, cholecystostomy is an entirely insufficient operation. Cholecystectomy is imperative and should be supplemented by hepatic drainage until a sterile culture is obtained as Garbat,[6] in his excellent monograph on the subject, has demonstrated. This is necessary not only for the sake of the patient, but also in the interests of the community.

Here, too, might be emphasized the possible danger to the individual of the chronically inflamed gall-bladder from an entirely different angle. I refer to the question of focal infection and its consequences. If diseased teeth or chronic tonsillar infection can produce arthritis, anemia, bronchial asthma or some other general constitutional disturbance it is quite rational to assume that a chronic cholecystitis may play a similar injurious role.

5. Postoperative Ventral Hernia and Hernia of the Gall-bladder. Obviously, the chances of a ventral hernia developing through the scar are greater when the gall-bladder has been drained than when it has been removed, and the wound closed more or less tightly (Cases IV and XXVIII). An occasional sequel of cholecystostomy is a ventral hernia, in which the gall-bladder becomes the contents of the hernial protrusion. The discomfort of the hernia is increased by the presence in the sac of this organ. The symptoms are much the same as those discussed in Group 3 under Adhesions, only possibly even more severe. Two cases of this nature follow:

Case XXX.—(No. 61, 1916.) Female, aged twenty-five years. She had been operated upon in 1915 for gall-stones. Several stones had been removed and the gall-bladder drained. Eight months after this operation she had an acute attack of pain in the region of the wound with cramps and vomiting after meals. The symptoms continued intermittently for four months, when she was admitted to my service and a large ventral hernia through the old scar was found. On January 6, 1916, she was operated upon by Dr. Carl Eggers for a repair of the hernia, who found in the hernial sac an adherent and somewhat distended gall-bladder (Fig. 15). A cholecystectomy and hernial plastic were done. Microscopical examination in this case also showed a chronic interstitial cholecystitis. The patient remained quite well until very recently, when she had an attack of pain in the same locality. This pain may have been due to adhesions, but in all probability was more of a neurosis because it subsided after a brief course of palliative therapy.

Case XXXI.—(No. 5766, 1921.) Female, aged forty-two years. In January, 1921, the gall-bladder was drained but no stones were

found. An enormous hernia developed through the scar. The patient was totally incapacitated by the pain and discomfort in this region. On September 29, 1921, I repaired the hernia by a plastic operation, but decided not to disturb the gall-bladder, which was imbedded in adhesions in the hernial sac. I felt that a cholecystectomy at this time might jeopardize the primary union of the hernial repair. The plastic healed solidly and the patient was greatly relieved for a time. Recently, she has again been troubled with symptoms seemingly referable to her gall-bladder and a cholecystectomy is now under advisement.

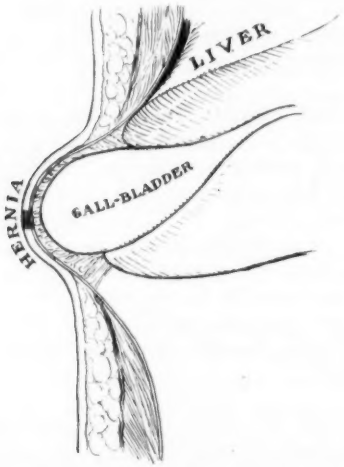


FIG. 15.—Case XXX. Hernia of gall-bladder. Adherent and somewhat distended gall-bladder in hernial sac.

6. DEVELOPMENT OF CARCINOMA IN THE RETAINED GALL-BLADDER. Although I have no personal experience with cancer developing after drainage of the gall-bladder, there are numerous reports in the literature of this occurrence (Fig. 16). Magoun and Renshaw,[13] in a recent paper from the Mayo Clinic on malignant disease of the gall-bladder, report 5 cases of carcinoma developing in the cholecystostomized gall-bladder in a series of 84 cases. In fact, it has even been shown that in many cases of inflamed gall-bladder, where this organ had been removed for what appeared to be merely an acute condition, there were precancerous or actually outspoken malignant changes demonstrable upon microscopical examination. This in itself, even ignoring the possibility of the development of carcinoma later in the degenerated and retained gall-bladder, is one of the most potent arguments in favor of primary cholecystectomy.

7. Recurrent Pancreatitis. It is now generally conceded that both acute and chronic pancreatitis are usually traceable to primary disease of the gall-bladder with or without stones. The pancreatic lesion is the result either of direct extension through the ducts or of secondary infection through the lymphatics. In all probability, some of my cases, grouped under (4.) Recurrent Cholecystitis, had complicating inflammatory lesions in the pancreas, which were in part responsible for the various digestive disturbances. The early treatment of chronic pancreatitis with or without jaundice, due to compression of the papilla of Vater, was cholecystostomy. Although this operation was originally strongly advocated by the Mayos, they were finally forced to admit that the cure affected by the drainage of the gall-bladder was only temporary, and that a recurrence was likely through reinfection from the gall-bladder when the fistula closed. They[16]

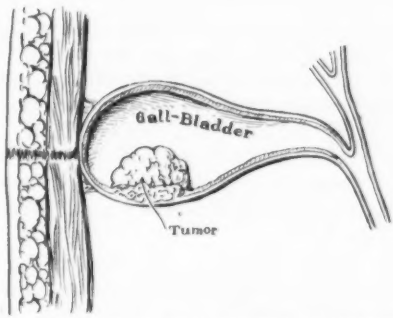


Fig. 16.—Carcinoma in the retained gall-bladder.

have since put themselves on record as advocating cholecystectomy as the only real curative procedure, primary in non-icteric and secondary in icteric cases.

8. Hepatitis. Under this heading I would like to refer briefly to the possibility of an inflammatory invasion of the liver with attendant disturbances of hepatic function resulting from the retention of a chronically inflamed gall-bladder. Aside from the possible extension of an acute gall-bladder suppuration into the bile ducts and liver, a chronic hepatitis, especially of the right lobe, frequently exists, apparently as a direct sequel to a chronic cholecystitis, the inflammation extending into the liver either by contiguity or via the lymphatics, the portal vein or the biliary system. Heyd[24] has very recently emphasized this association in primary cases. It is clear that if this relation can be substantiated, the danger is quite as great in retained, chronically infected gall-bladders, no matter by what path the disease travels.

**II. The Difficulties and Disadvantages of Secondary Cholecystectomy.** Having seen the clinical results of retention of the gall-bladder, let us now turn to the other side of the question and see what the surgeon faces when he tries to correct the sin of omission on the part of the previous operator—in many instances, himself—and attempts a secondary removal of the retained gall-bladder.

I have subdivided the difficulties and disadvantages of secondary cholecystectomy as follows:

1. Adhesions. Probably because of the great vascularity of the organs in this region, it is well known that the adhesions that form after operation in the right upper quadrant of the abdomen are particularly dense and extensive and that secondary operations on the gall-bladder and ducts often try the skill and patience of the most expert and experienced. Frequently, the entire upper surface of the liver, or at least its edge, and the gall-bladder are virtually glued to the anterior abdominal wall. The omentum is usually firmly attached to the gall-bladder; the pylorus, duodenum and hepatic flexure of the colon are likewise involved and conditions are often so complicated that surgical entrance into the abdominal cavity and proper orientation are very difficult (see Cases III, IV, V, VI, X, XI, XIII, XIV, XV, XVI, XVII, XVIII, XIX, XXVI, XXVII, XXVIII, XXX and XXXI). This not only applies to secondary cholecystectomy, but also to other surgical procedures in the neighborhood of the gall-bladder (see partial gastrectomy, Case XIX).

2. Injury to Other Organs. A corollary to the difficulties encountered from the presence of adhesions, more dense and extensive than usual, is the accidental injury to other important intra-abdominal structures. In many cases, the separation of the gall-bladder from surrounding structures is practically impossible without some serious damage being done, no matter how carefully the operation is performed.

I need but to refer to Case XI, in which, in merely trying to redrain the gall-bladder, the duodenum, which was densely adherent to the anterior abdominal wall, was inadvertently opened and drained, with eventually a fatal outcome (Fig. 17). This accident may have been avoidable, but, judging from the postmortem examination, if an actual cholecystectomy had been attempted, the gall-bladder was so shrunken and imbedded in adhesions that it would have been excessively difficult to locate it, and it was so adherent to the duodenum that an injury to that organ would have been an almost certain result.

In Case IV the duodenum and hepatic flexure of the colon were grown so firmly to the gall-bladder and under surface of the liver that only by the most careful sharp dissection could they be liberated, and the small, shrunken gall-bladder exposed (Fig. 18). It

seemed that this had been done with great success and without damage to the duodenum or colon, according to a very painstaking

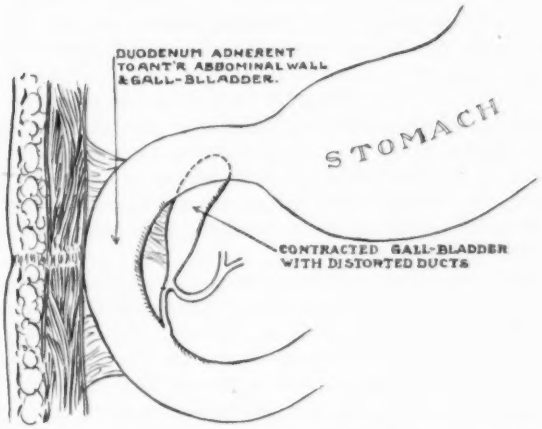


FIG. 17.—Case XI. Duodenum densely adherent to anterior abdominal wall and to shrunken gall-bladder. Distortion of ducts.

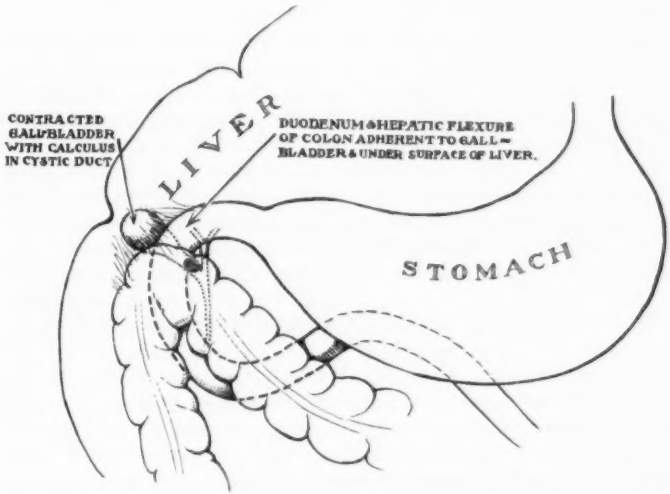


FIG. 18.—Case IV. Dense adhesions of duodenum and hepatic flexure of colon to gall-bladder and under surface of liver. Shrunken gall-bladder with impacted calculus in cystic duct.

inspection. Yet a week after operation, when the cigarette drain was removed, a fecal fistula of the hepatic flexure of the colon

developed. Although the development of this fistula was probably due, not to an actual operative perforation, but to erosion from the drains or invasion of the somewhat damaged gut wall by the infection, the primary cause and the end-result were the same. The fistula became mucocutaneous and required operative closure some months later.

In my series, it was my good fortune to have had no further accidents to other important abdominal organs. For the sake of completeness, however, I wish to emphasize the fact that, obviously, there is even much greater danger of seriously injuring the hepatic or common duct during one of these secondary operations, than at a primary cholecystectomy, where such injury is not an unusual occurrence.

3. Protracted Operation. Although the usual primary cholecystectomy requires a half to three-quarters of an hour, because of the adhesions and the disturbed anatomy, the secondary operations are generally very tedious affairs. Even a speedy operator can rarely finish such a case in less than an hour and a half or two hours, and if the difficulties are particularly marked, a longer time may be required. This is not without significance in some of the cases, where the patients are much run down from long-continued illness, particularly in those cases that have had long-standing biliary fistulæ.

4. Hemorrhage and Shock. Two other very serious factors are hemorrhage and shock, never to be regarded with indifference, but also of special seriousness in this class of cases. As already mentioned, the right hypochondrium is particularly vascular, and the bleeding in separating adhesions and loosening from the liver a firmly imbedded, shrivelled gall-bladder is often appalling. Frequently, the ligation of the cystic artery is next to impossible, and oozing from raw surfaces requires extensive tamponade (Cases V and XXVIII). This latter procedure, though necessary, predisposes to further adhesions, with the disadvantages that these entail. Unusual shock is an obvious sequence to the adhesions, protracted operation, additional operative traumatism and hemorrhage.

5. Postoperative Ventral Hernia. The possibility of the development of a postoperative ventral hernia is naturally increased by the relaparotomy. No comment is needed to explain this obvious fact. Case III is an illustration of this point. A large hernia has developed since the second operation, which will eventually require a third operation for its cure.

**Conclusions.** I think that it must be admitted from the observations that have been outlined, that it is justifiable to assume that the retained gall-bladder, at least one that has been drained, is a menace to the health, nay even to the life of the patient. Undoubtedly, some cases of cholecystostomy are cured,

but it has not been my fortune to have seen very many. The inference is obvious that if we operate on the gall-bladder—and it is more or less generally conceded today that gall-stones and most cases of cholecystitis, even without stones, should be treated surgically—then a primary cholecystectomy should be performed, if this is at all possible, irrespective of the degree of structural change in the gall-bladder itself. I would even go a step further. If, for any reason, either on account of the general condition of the patient or because of local difficulties, primary cholecystectomy cannot be performed and only cholecystostomy is done, this should be looked upon as an emergency procedure. A secondary cholecystectomy should be practised when the patient's condition has improved, unless there are specific contraindications. As a matter of fact, as can be seen from my experiences, reoperation is in many cases not a matter of choice but of compulsion. The one only exception to this rule is that mentioned in the beginning of this paper, namely, irremediable occlusion of the common duct, such as carcinoma of the head of the pancreas or impermeable stricture. Here the gall-bladder must be retained for the anastomosis with some part of the gastrointestinal tract. In chronic pancreatitis with jaundice, cholecystostomy should first be performed and, after the fistula has closed without symptoms so that the patency of the common duct is assured, secondary cholecystectomy should be undertaken. In chronic pancreatitis without jaundice, primary cholecystectomy is the operation indicated. In certain cases of so-called "silent" gall-stones, accidentally discovered during the course of a laparotomy for some other condition, where the gall-bladder is found to be comparatively normal, I have on several occasions practised "ideal cholecystotomy," closing the abdomen without drainage. This is at times a useful, alternate method, conserves the more or less healthy gall-bladder and obviates the disadvantages of cholecystostomy. Willis[20, 21] has very recently revived interest in this procedure and recommends it when indicated.

I have yet to see any harm come from the absence of the gall-bladder, in spite of the various theoretical objections that have been advanced against its removal. With very few exceptions, the many cases of cholecystectomy that I have observed have been promptly and definitely cured by the operative procedure, and never have I seen the slightest recognizable functional disturbance result from the loss of the gall-bladder, even when this organ was not seriously diseased at the time of operation. Where the gall-bladder is badly diseased, and particularly where the cystic duct is occluded, the gall-bladder is worse than functionless, anyway.

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sions. I believe the reverse to be the truth and that the retention of the diseased gall-bladder will produce many more and denser adhesions than its removal. I believe this to be particularly true with the technic which I am now using, with complete success up to date, and which has for some time been recommended by many, though not universally approved. I refer to cholecystectomy without drainage. I might here emphasize that the period of convalescence in cholecystectomy, particularly the wound healing, is much shorter than in cholecystostomy, and will be still further curtailed by this non-drainage operation. Incidentally, the complete closure of the abdominal wound without drainage is clearly not as feasible in secondary as in primary cholecystectomy.

May I conclude my plea for primary cholecystectomy with the statement that I agree with those surgeons who believe that the gall-bladder, found diseased at operation, should no more be left in the abdominal cavity than should the diseased appendix. Unless this maxim is followed, as a general rule, I feel that the surgeon will inexcusably place the future health, and even the life, of many of his patients in serious and unnecessary jeopardy.

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## ASSOCIATED ACUTE THORACIC AND ABDOMINAL DISEASE: WITH REPORT OF A CASE OF PNEUMONIA AND APPENDICITIS AT THE SAME TIME.*

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Nearly every hospital has the tradition of an early pneumonia being mistaken for an acute appendicitis because of abdominal pain and resistance. Operation revealed a normal appendix and a normal abdomen, and the case proved to be a frank pneumonia. An early pneumonia, with its accompanying acute fibrinous pleurisy with referred pain, may simulate any acute condition below the diaphragm. To put the point differently, abdominal pain and rigidity do not mean that there is abdominal disease, much less an acute abdominal condition. On the contrary, and under the same circumstances, it is often difficult to deny that acute abdominal trouble is present. Further, the laboratory offers practically no assistance in the differentiation, because there is usually a leukocytosis with high polymorphonuclear count both in pneumonia and in the acute abdomen.

In the following case, both a pneumonia and an appendicitis were present, and probably began at the same time, as the case is now viewed with the added accuracy of hindsight. The simple telling of the story will add emphasis to Pottenger's[1] recent statement that "Diagnosis is a process of reasoning." It shows the pitfalls in a concurrent acute abdomen and acute thorax. Truly, here, experience is fallacious and judgment difficult.

A well-developed girl, aged thirteen years, entered the Wesley Hospital on the afternoon of August 26, 1921, with a complaint of pain in the lower right abdomen. She had been well until August 11, when she developed a severe cold, which lingered until August 24,

* Annual Oration on Medicine of the Medical Association of the State of Mississippi, May 10, 1922.

when she had a severe chill and high fever. In the afternoon of the next day, an acute epigastric pain developed and, on the day of entrance, it had localized in the right side of the abdomen, worse from above downward and culminating in the appendix region. On entrance, the subjective pain was greatest to the right of the umbilicus, though the entire right abdomen was resistant and most painful upon pressure over McBurney's point. Temperature, 103°; pulse, 140; respiration, 32. On account of her abdominal condition she was entered in the surgical service, and Dr. C. E. Dowman saw her at 5 P.M. His notes were as follows: "Percussion note definitely higher over lower half of right lung. Vocal fremitus slightly increased posteriorly right. Breath sounds: Expiratory sounds rather prolonged and somewhat harsh over lower right side. Abdomen: Marked tenderness over right lower quadrant. No mass felt. Hyperesthesia test absent. Impression: Case is probably one of the right lobar pneumonia with referred pain in the appendix region. A true appendicitis, however, should be kept in mind. Have internist see patient."

My notes after examination, one hour later, were as follows: "Patient has a tachypnea of 36, rhythmic; pulse, 128. Absent to decreased fremitus midright scapula downward, increased above. Squeaking rales, rhonchi, few fine crepitant rales fifth space anteriorly outward and backward to right back. Acute fibrinous pleurisy, probably right anterior axillary line. Referred abdominal pain. Cold preceded illness. Would suspect frank pneumonia signs by morning."

Her urine was 1026, with a heavy trace of albumin. The leukocyte count was 17,600; polymorphonuclears, 83 per cent; small lymphocytes, 15 per cent; large lymphocytes, 2 per cent. An ice-bag was kept constantly on the right lower quadrant. On the next day, August 27, a bronchopneumonia, involving the entire lower right lobe was present, and the abdominal pain and rigidity were greatly decreased. The abdominal improvement was interpreted as a result of the ice-bag and the care of the patient. Now, we believe it was due to the rupture of the appendix. Coughing had begun. Temperature ranged from 99° to 101°; pulse, from 88 to 110; respiration, 20 to 24. On August 29, she complained of pain in the entire abdomen, with increased pain on pressure over the appendix and upward. On August 30, coughing gave her abdominal pain, and by 8 P.M. it had localized in the lower right quadrant. On August 31, the abdominal pain was more severe; epistaxis occurred and vomiting, with a few blood streaks. The cough accentuated the pain, but it was clearly evident that there was an abdominal lesion as well as a pneumonia. The hyperesthesia test, elicited by drawing a pin over the abdomen, gave a pronounced reaction over the appendix region. The progress of the pneumonia was satisfactory and her general condition fair. On

September 2, the leukocyte count had dropped to 7000, with a normal differential count. The patient looked better, temperature and pulse were normal and respiration was 26. Right lower quadrant rigid; decided localization, with mass sensation upon palpation over cæcum. Breathing all thoracic. Operation was done at once under local anesthesia, and a large walled-off retrocecal appendiceal abscess was found. The appendix was not removed. Stab drainage in right flank. Morphia was necessary to relieve the abdominal pain from the cough of the pneumonia. Patient was septic with continued fever, rapid pulse and prostration. Calomel was given on September 5 and 6, with much improvement. Temperature, pulse and respiration were normal on September 8. Recovery uneventful thereafter.

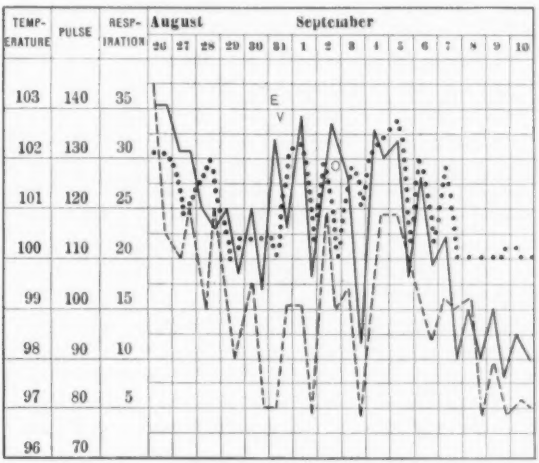


FIG. 1.—Solid line, temperature; broken line, pulse; dotted line, respiration; V, vomiting; E, epistaxis; O, operation.

There is evidently much more to this case than a simple case of pneumonia or appendicitis. The patient had a severe cold for thirteen days, and then suddenly had a chill and fever, with signs of pneumonia and appendicitis. We believe both began at the same time, and that they were the local manifestations of a general septicemia. Had there been no lung signs, the diagnosis would have been acute appendicitis. In the beginning, we thought the abdominal condition was due to the referred pleural pain of the pneumonia. Unfortunately, a blood culture was not taken. The sputum and pus from the appendiceal abscess both contain staphylococci and short chain streptococci. No pleural friction rub was ever heard. The abdominal pain began in the epigastrium,

even though the appendix was retrocecal. The abdominal pain was probably due entirely to the appendicitis and there was probably no referred pain from the thorax at any time.

Cabot's case record No. 7363 (Massachusetts General Hospital), is an account of a similar case, except that the appendix seemed the only organ involved. It was removed, but a right bronchopneumonia was at once evident and a mild jaundice as well. At necropsy, there was a fibrinous pleurisy and a fibrinous pericarditis. Here was a blood-stream infection, a bacteriemia, that was the beginning of the pathological mischief in lung, appendix, liver and pericardium. The pneumococcus was the "criminal." Cabot wisely

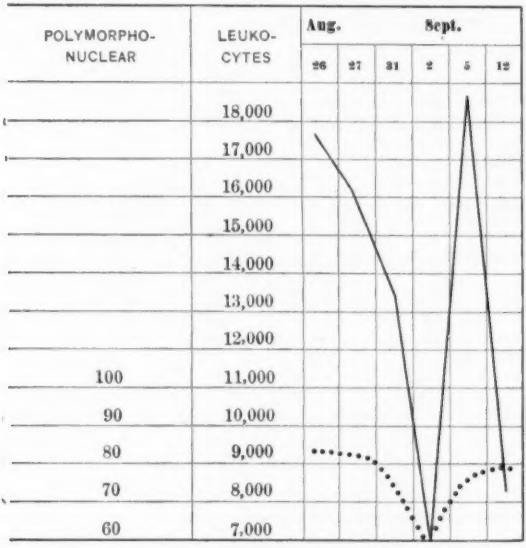


FIG. 2.—Solid line, leukocytes; dotted line, polymorphonuclear leukocytes; operation, September 2.

says, in discussing this case, "I believe we shall see a great deal more of the doctrine of general septicemia, with local manifestations or without." W. W. Herrick[2] has shown that epidemic meningitis is preceded by a general invasion of the blood stream, or stage of meningococcic sepsis, and that in some cases the infection remains a sepsis and never localizes in the meninges or elsewhere. It is significant that measles, meningitis and influenza are so often complicated by bronchopneumonia. We saw one soldier who had measles, meningitis, bronchopneumonia and erysipelas, in the order named (the last three concurrently), and he recovered. In Cabot's case and in ours, the pneumonia was bronchial in type.

Two recent cases bear upon general sepsis: a little girl, aged seven years, had chronic infectious tonsillitis, endocarditis with mitral incompetency, acute rheumatic fever and chorea major at the same time. She recovered with, of course, a damaged mitral valve. A woman, aged forty years, had an acute suppurative cholecystitis with a polyarticular arthritis, and the arthritis disappeared after a tonsillectomy and a cholecystectomy. Bindi[3] reports a case of acute arthritis associated with an acute appendicitis.

We have, in recent years, been so overwhelmed with the importance of the doctrine of focal infections, and so intense in the search for the focus, that we have probably not accentuated sufficiently the importance of the blood stream in the dissemination of the bacteria, whether known or unknown. Ports of entry of focal infections through the blood stream to the tissues are of two kinds: (*a*) Peripheral and relatively easily demonstrable foci, as the teeth, tonsils, mouth, sinuses, skin, cervix, urethra and prostate; (*b*) cryptic foci, relatively impossible to demonstrate, as the mucosa and alveolar cells of the bronchial tree and the intestinal mucosa. The hidden potential foci are far more numerous than the peripheral foci. In either case, the blood stream may be a culture medium for bacterial growth as well as a distributing agent for the elective localization of the bacteria in different organs. It is meningococcic sepsis when the meningococci remain in the blood; when they localize in the meninges, it is meningitis. In the case reported, the bacteria probably localized in the lung and appendix after a stage of sepsis, following entrance from an unknown focus. Hidden sepsis is a phrase of no mean value and emphasizes the importance of careful and repeated blood cultures. General sepsis may be present without pus, or discoverable focus, or port of entry into the blood stream, once the bacteria enter the closed circulation. The blood stream does the rest, with or without subsequent localization.

The doctrine of referred pain is one of ever increasing importance. Here was an acute abdominal condition that was taken to be a referred pain from acute thoracic disease. We have so fallen into the use of instruments of precision in the study of a case, that we may overlook the precision of referred pain or overestimate it entirely. James MacKenzie's book on *Symptoms and Their Interpretation* should be familiar to every clinician. There is enough time in every case of appendicitis to be sure it is appendicitis, and not a referred pain.

A few simple facts are of aid in reaching a conclusion in a problem of referred thoracic pain: The lungs give rise to no sensation of pain. The pleura is insensitive to probing or stimulation. The pain in a pneumonia, whether local or referred, is due to the involvement of the pleura, usually as an acute fibrinous pleurisy. Little is known of the nerve supply to the pleura. The intercostal

muscles over the affected lung are tender upon pressure in a painful pneumonia chest. "The most severe pain occurs in the movement of respiration and is due to the peripheral contraction of the intercostal muscles" (MacKenzie). The intercostal muscles over a painful pneumonia are in a state of rigid contraction. The pain is often localized in the anterior axillary line, where the visceral, parietal and diaphragmatic pleura make their maximal excursion. The pain may be referred to the abdomen reflexly through the intercostal nerves.

The skin and muscles of the abdomen are supplied by the anterior branches of the six lower dorsal nerves and the ilioinguinal and the iliohypogastric from the lumbar plexus. The intercostal muscles of the thorax are supplied by the second and third cervical and the second, third and fourth dorsal; the diaphragm by the phrenic from the fourth and fifth cervical. The spasm of the intercostal muscles is a viscero-motor reflex—pleura to cord to intercostal muscle. The pain in the chest is a viscero-sensory reflex, due to the painful contraction of the muscle on its contained nerves—pleura to cord to muscle.

Both the abdominal muscles and the skin overlying them are supplied by the spinal nerves. The referred pain in a pneumonia is, therefore, a viscero-sensory reflex—from pleura through thoracic intercostal nerves to cord, and then a shunting down the cord to the lower dorsal nerves to abdominal skin, and painful nerves in contracted muscles, The pain in diaphragmatic pleurisy is a viscero-sensory reflex to the shoulder crest. The referred pain in acute thoracic disease may localize in the upper abdomen and simulate gall-bladder disease or ruptured gastric or duodenal ulcer. To further complicate the problem, referred pain may shift up and down the abdominal wall.

The spinal nerves supply the surface, and the sympathetic the viscera beneath the surface of the abdomen. The hyperesthetic, painful, resistant or rigid and abdominal muscles in appendicitis are entirely due to reflex action. The cold hand upon the warm abdomen causes instant contraction of skin and underlying muscles.

Pain in the epigastrium in gall-bladder disease or umbilical region in appendicitis seems to appear there because these parts are derived from the primary embryological median tube and peristaltic pain also is usually referred to the median line. The nerves to the appendix are from the mesenteric plexus, and are intimately connected with the dorsal and lumbar spinal nerves. In appendicitis, there is reflexly a viscero-motor reflex with spasm of the erector spinæ in the right flank and spasm of the psoas with tendency to flex the right thigh.

**Conclusions.** 1. In concurrent acute thoracic and acute abdominal disease, it is very difficult to separate the signs and symptoms of one from the other, on account of the doctrine of referred pain.

The laboratory is of little assistance. It is a matter of clinical judgment.

2. Even an early pneumonia, through referred pain to the abdomen, may simulate any acute condition below the diaphragm, and yet the abdomen be normal. Hesitancy here and observation are of value.

3. Acute concurrent inflammations, as illustrated by the case reported, in different organs or different systems of organs intimate a blood-stream infection, and the acute diseases are its local manifestations.

4. No acute abdominal trouble should be operated upon until a real examination of the lungs has been made. Where there is a doubt between the acute thoracic and the acute abdominal condition or both concurrently, a policy of watchful clinical waiting is in order. If still an operation seems imperative, local anesthesia will probably lessen the thoracic danger.

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## PRIMARY LYMPHOBLASTOMA OF THE STOMACH.

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Tumors of the stomach, carcinoma excepted, are comparatively infrequent. The term lymphosarcoma signifies a malignant tumor of mesenchymal origin in which the tumor cell is of the lymphocyte series. Lymphosarcoma may occur anywhere in the lymphatic system (including the lymphoid tissue of the gastric wall). A rational division of lymphosarcoma is into: (1) A group of cases in which the predominating type cell is the small round cell which corresponds to the lymphocyte of the circulating blood; and (2) a group in which the predominating type cell is not the lymphocyte but its ancestral element—the larger, more cytoplasm-rich, hyperchromatic lymphoblast as it occurs normally in the germinal centers of lymph nodes. To the first group the name *lymphocytoma* may be applied; to the second group is applied the name *lymphoblastoma* (Ribbert,[1] Delafield and Prudden[2]). Some cases of lymphosarcoma clearly belong to the first of these groups and other cases clearly to the second group, but between the two rather

clear-cut extremes there are overlapping cases—cases in which there is such a free admixture of smaller cells approximating lymphocytes and of the larger and more immature lymphoblasts that satisfactory classification may not be possible. Ribbert would discard the term lymphosarcoma as applied to either group, reserving the term sarcoma for tumors of supporting connective tissue. By pathologists in general the tendency is to include also under the name of lymphosarcoma the tumor masses of lymphatic leukemia and Hodgkin's disease. Pathologists in general have not accepted the views of Frankel and Much, Bunting and Yates, Rosenow and others as to the bacterial origin and granulomatous nature of Hodgkin's disease. On the contrary, the drift of opinion is to the view that Hodgkin's disease is essentially neoplastic (lymphosarcomatous) in nature.

The literature of primary lymphosarcoma of the stomach is scant, and in case reports very few, if any, attempts have been made to draw a line between lymphocytoma and lymphoblastoma. There are in the Surgeon-General's Library clinical or autopsy reports in German by Török (1892)[3], Sternberg (1907),[4] Saltikow (1910)[5], Ruppert (1912),[6] and Krabbel (1918).[7] Török's case was in a woman, aged twenty-one years, in whom almost two-thirds of the stomach and three regional glands were removed. The tumor was the size of a fist involving the greater curvature toward the fundus and densely adherent to the parietal peritoneum. The patient was seemingly well nearly two months after operation. Sternberg comments upon the almost universal rule of dilatation of the stomach in the presence of lymphosarcoma. In Saltikow's report of 3 autopsies, all in elderly women, (aged sixty-seven, sixty eight and seventy-four years), the stomach was normal in size in 1 and reduced in 2.

Ruppert's interesting report is of a case in a woman, aged seventy-two years, in good health, for whom he had done a nearly complete gastrectomy fourteen years previously. The movable tumor was as large as a child's head and occupied almost the whole length of the stomach except a strip of three fingers' width at the fundus. There were also numerous glands involved in the great and small omentum and at the cardia. The wall of the stomach was infiltrated in almost its entirety. Ruppert comments upon the extreme malignancy of lymphosarcoma and states that he could find in all the literature but 12 operated gastric cases, of which 5 died from the operation and of the remainder none had survived as long as his case.

Krabbel's report is of a case autopsied after exploratory laparotomy for acute *dynamic* intestinal obstruction. The whole fundus and the lesser curvature were extensively infiltrated and there were two ulcerated areas, but the pylorus was not obstructed. Metastases were very extensive. The brain and cord were not

examined, but cerebral symptoms clinically resembling those of bulbar paralysis strongly suggested metastases in the central nervous system. The immediate cause of death was considered to be sudden heart failure due to myocardial metastases. Krabbel calls attention to the infrequency of primary lymphosarcoma of the stomach, stating that Pappert in his thesis in 1911, could find but 26 cases in the German and foreign literature. Krabbel believes that the disease runs a long symptomless course prior to the onset of serious symptoms, for which reason early operations and operative cures have been rare. He states that pyloric stenosis is extremely rare. He also observed that in a majority of cases reported cachexia was completely absent or appeared late and suddenly. In his case the patient, a teamster, continued at his duties until within less than a month of death.

Reports of but 2 cases in French could be found, 1 by Ferlin (1907)[8] in a man, aged forty-seven years, who for a long time had complained of stomach symptoms with hemorrhage now and again and in whom there eventually developed a phlebitis in both legs; the other by Gilbert (1912)[9] in a man, aged fifty years, who also had hemorrhage. Both cases were autopsied and examined histologically.

Only 2 cases could be found in English literature, reported by Hadden (1886)[10] and Alson (1886)[11].

American literature is likewise limited: in 1862, Jackson[12] showed an undiagnosed postmortem specimen described as "a very anomalous tumor found in the parietes of the stomach," a detailed account of which suggests primary lymphosarcoma. This case appears to be the first recorded.

Scott and Forman (1916)[13] reported a case of diffuse gastric neoplasm with metastases in the lymph nodes along the lesser curvature and about the head and along the upper margin of the pancreas, which was studied histologically and classified as Hodgkin's disease of the stomach.

Broders and Mahle (1921)[14] reported 12 cases of primary lymphosarcoma of the stomach occurring in the Mayo Clinic from January 1, 1913, to December 1, 1920. According to their records (Mayo Clinic) primary lymphosarcoma of the stomach as compared with carcinoma occurs in the proportion of 1 to 68; 11 of their cases were in males. The age limits were from sixteen to sixty-two years. The clinical diagnosis in 7 was carcinoma; the remaining 5 were variously diagnosed, but not one as lymphoblastoma or sarcoma.

In a private communication of February 23, 1921, F. B. Mallory states that during the past twenty-five years there have been but 3 cases of lymphoblastoma of the stomach in the Boston City Hospital.

Lymphoblastoma of the stomach is very malignant, as would

be expected in view of the large cytoplasmic content and immaturity of the component cells. The tumor grows rapidly and tends to infiltrate extensively. In microscopical slides numerous mitoses are apt to be seen, especially in metastases. In nearly all, if not in all, of the autopsied cases, extensive metastases have been found—in some cases so generalized as to involve most of the organs of the body. The regional lymph nodes are most frequently and first involved, but other nodes, the omentum, mesentery, intestine, liver, spleen, pancreas, kidneys, diaphragm, pleuræ and heart are apt to suffer. It is probable that even the central nervous system may be invaded. Metastasis occurs through the lymph current and, it may be, in some cases also through the blood current.

The clinical diagnosis is difficult. In a review of all case reports available, I did not find a single case in which the clinical diagnosis was made. The usual diagnosis was carcinoma. In its early stage the tumor is most frequently situated in the pyloric end and upon chemical analysis of the gastric contents the findings are like those of cancer.

Some clinical features which may have a diagnostic value are: (1) The age of the patient. A considerable percentage of the reported cases has been in patients too young for carcinoma. (2) The absence of pyloric stenosis. In several of the cases reported the absence of obstruction was noted. In the case below reported, although the primary tumor was very close to the pylorus, the outlet was not notably narrowed; and although after gastrojejunostomy, metastasis occurred proximal to it, the ring was not encroached upon; and although the distal end of the esophagus became seriously involved, its lumen was not obstructed. (3) Absence of cachexia or its very late appearance. This fact was also commented upon in some of the case reports. (4) A greater tendency in some cases to copious bleeding than ordinarily is present in carcinoma. (5) Possibly a period of more or less prolonged ill health prior to the onset of severe symptoms. Krabbel called attention to this feature.

It is quite likely that primary lymphosarcoma of the stomach is not as rare as the literature would indicate; the Mayo Clinic records tend to this conclusion. Doubtless many cases of gastric tumor diagnosed as carcinoma would have proved to be lymphosarcoma if studied histologically.

In the case to be reported presently it seemed to me that it might be of some interest to apply to the patient's serum the specific ferment test (dialysis procedure) of Abderhalden, the object being to determine whether in case of a positive reaction to a fragment of the patient's own tumor (to be obtained at autopsy), there would occur a similar reaction to such other tumors of the lymphocyte series as it might be possible to secure. Accordingly blood was

taken by Dr. O. B. Hunter five days before death and the serum preserved under proper conditions. Dr. Hunter kindly consented to make the tests in his laboratory at the George Washington University Medical School. Unfortunately the only additional material which could be obtained during the period of activity of the serum was a fresh fragment of lymphocytoma sent to me by Dr. L. F. Barker. The two tumors reacted positively, that is, showed the presence of a defense ferment, which correspondence tended to establish their serological identity as well as to confirm their close pathological relationship.

As to the prognosis little need be said except that the only cured case which I could find of record was the case of Ruppert previously mentioned. Doubtless the problem of cure is more or less analogous to the problem of gastric cancer, if the disease were recognizable in its incipiency and were dealt with radically there would be more cures.

Case Report. F. W. T., aged sixty years; lawyer; American; married; resident of Washington, D.C.

*Family History.* Negative for malignant disease.

*Previous Personal History.* (September 22, 1919.) No serious illness or injury during adult life and health excellent, with average weight of 175 pounds, until last two years; during past two years mild dyspeptic symptoms from time to time—capricious appetite, with eructations of gas and flatulency; no pain, nausea, vomiting or diarrhea; mildly constipated at times; during same period gradual loss of weight, in all about 30 pounds, and diminishing endurance; otherwise general health satisfactory and there has been no interruption of work; habits always temperate.

*Physical Examination.* Height, 5 feet 10 inches, weight, 147 pounds. Head and neck negative except for some suspicious teeth—tonsils appear normal; chest negative except for slight enlargement of heart to left and moderate accentuation of second aortic sound; abdomen of normal contour, everywhere soft, no tenderness, no palpable mass; liver not palpable below normal limits; spleen not palpable; regions of pylorus, gall-bladder and appendix negative; kidneys in good position; peripheral arteries moderately stiffened; blood-pressure 105 to 186; a few palpable lymph nodes in either groin; temperature normal; general appearance that of moderate malnutrition and a moderate degree of anemia.

Blood examination, erythrocytes, 4,400,000; leukocytes, 7600; hemoglobin 78 per cent; Wassermann, negative. The morning urine showed no indican or other abnormality. The stool was well digested and showed no excess of mucus and no gross or occult blood, parasites or ova.

Roentgen-ray examination of the upper digestive tract (Christie, September 24, 1919): abscesses involving roots of upper left first

molar and very marked pyorrheal absorption about all lower incisors; the stomach is ptotic, but normal in contour, motility, mobility and time of evacuation; no deformity of pylorus or duodenal cap; no shadows of gall stones or other evidence of gall-bladder disease.

A diagnosis was made of oral infection and a moderate general arteriosclerosis.

The patient was not seen from September 26, 1919, to April 29, 1920.

*Condition April* 29, 1920. The symptoms since former examination have been in the main a continuance of those previously present, except that recently there has been a more rapid loss of weight. The general condition has greatly deteriorated—the patient is thin and sallow, but not distinctly cachectic; weight 132 pounds. Examination of abdomen shows the presence of a definite, firm, tender mass in the region of the pylorus about the size of a small orange cut in two transversely, which moves to and fro with excursions of the diaphragm. Gastric contents: complete absence of free hydrochloric acid, total acidity 5, a trace of lactic acid and a small amount of gross blood. The stool shows occult blood. A diagnosis of pyloric carcinoma seems probable. Although the tumor is obviously very close to, if it does not actually involve, the outlet, there is no evidence of obstruction—solid food is taken without a great deal of discomfort and there has been no vomiting.

Roentgen-ray examination of stomach, May 5, 1920 (Christie), shows a large filling-defect involving the pyloric end, considered to be typical of carcinoma.

The patient was admitted to the George Washington University Hospital, May 8, 1920, and two days later the abdomen was opened by Dr. William C. Borden. A firm, circumscribed, somewhat nodular gastric tumor approximately 7 by 8 cm. in size was found, involving both curvatures and both walls and reaching very close to, though not involving, the pylorus. There were two moderately enlarged gastro-colic glands; otherwise no discoverable metastases. The liver and pancreas appeared normal. A posterior gastro-jejunostomy was done with the anastomosis as far away as practicable from the growth. Recovery from operation was excellent. Fifteen days after operation roentgen-ray examination showed an almost empty stomach one hour after the barium meal, evacuation taking place entirely through the ring of the anastomosis. Sixteen days after operation the abdomen was again opened by Dr. Borden. The tumor had increased considerably in size; its rate of growth was impressive. Something more than the distal third of the stomach with the proximal end of the duodenum and the two enlarged gastro-colic glands were removed *en masse*. It was possible to make the gastric incision well away from the tumor-mass without encroaching unduly upon the opening of the gastro-enterostomy. The stomach wall beyond the limits of the

mass did not seem to be infiltrated. The operative diagnosis was carcinoma. The operation was well borne and recovery uneventful. On June 6 (twelfth day after gastrectomy), the patient was returned to his home in remarkably good condition, although his weight had dropped to 117 pounds. From then he ate well and with complete comfort and gained weight rapidly. Blood examination July 31: Erythrocytes, 4,200,000; leukocytes, 6500; hemoglobin 66 per cent (Dare); polymorphonuclears, 70 per cent; lymphocytes, 23 per cent; mononuclears and transitionals, 3 per cent; eosinophiles 3 per cent; myelocytes, 1 per cent; red cells show considerable achromia, moderate anisocytosis, moderate poikilocytosis and some tendency to polychromatophilia in an occasional cell; no nucleated reds. On September 17, the weight was 134 pounds, or 2 pounds more than preoperative weight.

*Note of September* 20: General appearance fair; above navel to left of median line there is a doubtful small mass; liver, spleen and lymph nodes, other than those in groins, negative.

*Note of October* 21: Appetite poor, not much gas, no nausea or vomiting; complaint of pain and tightness in lower part of chest —no cough; tongue clean; pulse rate, 96; temperature, 101.5°; impairment of resonance, diminished breath sounds and moist rales over bases of lungs; mass previously noted as doubtful is now easily palpable between left costal margin and navel, quite firm, movable.

On October 24, there were many evidences of severe hemorrhage: Pallor, rapid pulse, subnormal temperature, cold extremities, an attack of syncope on rising, and so on. The general condition rapidly went from bad to worse. On two or three occasions some moderately bright blood was vomited and there were some black stools. Death occurred October 27, five months and one day after gastrectomy and approximately thirteen months after stomach had been found normal on physical examination and radiographically. The immediate cause of death was massive hemorrhage.

Pathology. 1. *Specimen Removed at Operation.* The specimen consists of distal portion of stomach, proximal extremity of duodenum and a portion of gastro-colic omentum. Dimensions of gastric portion containing tumor are 14.5 cm. in length by 8.5 cm. in width, with a capacity of 250 cc. The neoplasm involves anterior and posterior surfaces and both curvatures. The two surfaces and inferior curvature are extensively thickened, hard and nodular; the superior curvature is also thickened, but to a less degree. In the omental portion of specimen there are two moderately enlarged lymph nodes and several nodes of smaller size. The gross specimen is suggestive of a diffuse infiltrating carcinoma. After fixation in 10 per cent formalin the infiltrated walls are very friable and fracture easily on traction or bending. The nodular infiltration involves all coats from mucosa to peritoneum,

but without breaking through the latter. On the mucous surface there are a number of undulating projections, hard and firm, with numerous small grayish nodules—the whole covered with a brownish-black, flaky exudate. There is no ulceration. On the external aspect there are similar wavy projections, but none of the smaller nodulations; the peritoneal coat is comparatively smooth.

The tumor cuts with firm uniform consistency and appears as a white solid growth involving the entire thickness of the gastric wall, with complete obliteration of the outlines of the mucous, connective tissue and muscular tunics. The entire growth appears to be well distal to the line of amputation. The excised glands show on section the same white uniform appearance and firm consistency.

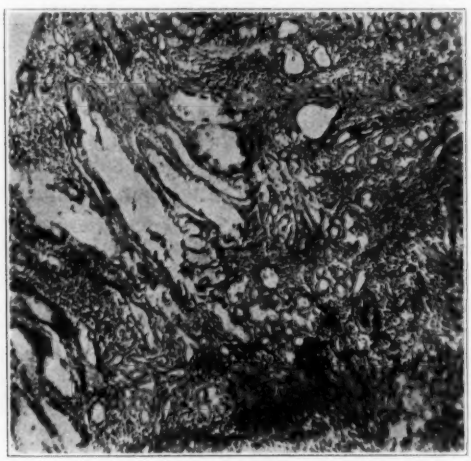

FIG. 1.—Microphotograph showing lymphoblastic growth infiltrating and obliterating gastric glands.

Microscopical sections from central part of growth show extensive lymphoblastic proliferation, completely obliterating the mucous, submucous, and muscular coats, with absolute loss of all of the normal histological structures. The thickness of the growth varies from 5 mm. to 20 mm. Toward the periphery the lymphoblastic growth shows macroscopically a rather sharp line of demarcation between it and the normal mucous membrane and musculature, but microspically there is a well defined diffuse, but scanty, lymphoblastic infiltration into these coats as well as the submucosa.

Cytological study shows a great predominance of large hyperchromatic, lymphoblastic cells, atypical in arrangement and structure, closely packed together, with little supporting connective

tissue. There are no distinct giant cell formations, although there is some tendency to nuclear group accumulations with little

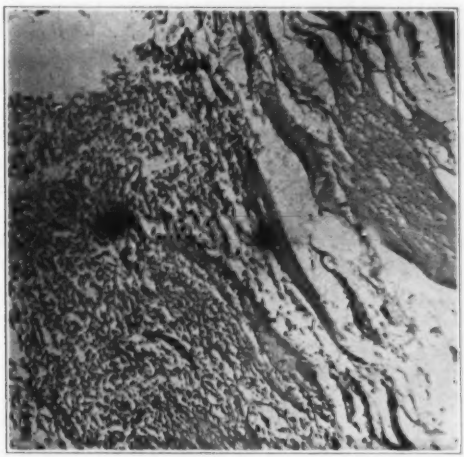

FIG. 2.—Microphotograph showing lymphoblastic growth infiltrating and obliterating gastric musculature.

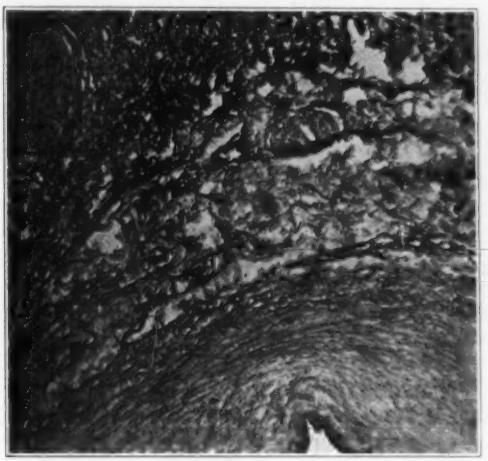


FIG. 3.—Microphotograph showing left gastric artery with perivascular infiltration only. *a*, lumen of vessel; *b*, media; *c*, adventitia, showing lymphoblastic infiltration.

cytoplasmic production. A few esoinophiles are found scattered through the tumor in various areas. Some lymphocytes are pres-

ent with small round pyknotic nuclei and little cytoplasm, but are comparatively scant. Endothelial proliferation and fibroblastic formation are at a minumum. New-formed capillaries are moderately abundant and there are many vascular spaces with no apparent endothelial lining. Some polymorphonuclear leukocytes are found in the tissue, but are not numerous; they are found more particularly toward the mucous surface and in the regions of the larger capillaries. Numerous mitotic figures are found throughout the mass and there is extensive hyperchromatosis of the lymphoblastic nuclei.

Sections from the lymph nodes show essentially the same histological structure as the primary growth.

2. *Partial Autopsy (Incomplete for Lack of Consent) Done Three Hours After Death.* Stomach, liver (both lobes), omentum, proximal part of jejunum (region of gastro-enterostomy) and a large part of the transverse colon are densely adherent to parietal peritoneum in line of operative incision and bilateral to it. The gall-bladder is incarcerated in a mass of adhesions. The proximal part of lesser curvature of stomach, the proximal part of the lesser peritoneal sac and the transverse fissure of the liver are filled with adhesions and new growth. There are many enlarged abdominal lymph glands including the paracardial, superior gastric, hepatic and pancreatico-lineal groups. No enlarged pyloric or inferior gastric glands can be found. Removal of these groups appears to have been completely effected by operation. The retroperitoneal glands do not seem to be involved. Both lobes of liver and the pancreas contain new growth. The spleen, although firmly attached to the stomach, contains no gross mass. By palpating through incision in diaphragm, glands of the posterior mediastinum are found enlarged and nodules are felt in left lung in region of hilus.

Examination of stomach after removal shows perfect healing of distal extremity (line of amputation) without macroscopical evidence of recurrence of growth in that vicinity. The ring corresponding to surgical junction of stomach and jejunum is 3.5 cm. in its longest diameter and is covered with apparently normal mucous membrane. The stomach and small and large intestine contain a very large volume of fluid and clotted blood. At the proximal end of the superior curvature of the stomach is a hard mass 6 cm. in length by 2.5 cm. in thickness, from which there is a well-defined extension upward involving the right lateral wall of the lower end of esophagus. The esophageal lumen is not appreciably narrowed. From the distal portion of the mass, but reaching close to the proximal end of the superior curvature, there is another extension hanging in a more or less pedunculated manner into the cavity of the stomach. In the latter extension the distal portion of the left gastric (coronary) artery is found with numerous

eroded branches from which very extensive bleeding has occurred. The remaining portions of the stomach show no evidence of neo-

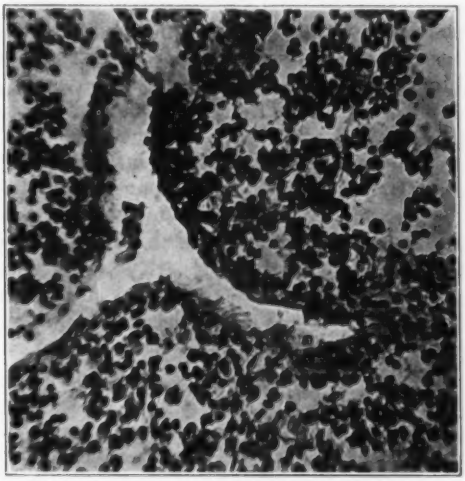

FIG. 4.—Microphotograph from operative specimen, showing rich, lymphoblastic growth and embryonic bloodvessel.

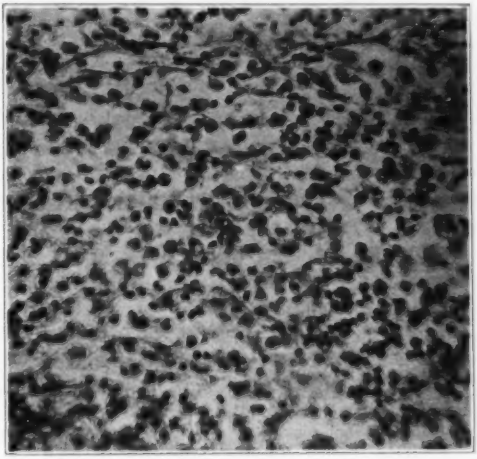

FIG. 5.—Microphotograph from autopsy specimen, showing same richly cellular growth with mitotic figures, similar to operative specimen.

plasm and no nodules can be found in the distal portion of the jejunum, the ileum or the colon. The mass in the stomach clearly represents the initial recurrence. The masses in the liver

and pancreas appear to be direct extensions. The numerous metastases noted (*e. g.*, in the mediastinal glands) have obviously occurred through the lymph current.

Microscopical sections from various specimens show essentially the same lymphoblastic proliferation and infiltration as the operative specimen. Curiously the trunk of the left gastric artery is surrounded by the growth, with some infiltration of the adventitia, but without involvement of the media and without obstruction of its lumen; some of its smaller branches are eroded. A few nerves in the immediate neighborhood show some infiltration of the epineurium, but no invasion of the medullary structure.

The pendulous mass in cavity of stomach consists of fibrin, lymphoblastic and polymorphonuclear infiltrations, some connective tissue and many bloodvessels. The latter show evidence of extensive hemorrhage and are the seat of fatal bleeding. The outline of some of the lower mediastinal glands can only be made out by their pigmentary deposits and capsule ghosts.*

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## NON-SPECIFIC GRANULOMATA OF THE INTESTINE.†

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Our purpose in this paper is to describe the pathological and some of the clinical features of a malady which, we have reason

* I am greatly indebted to Dr. O. B. Hunter for his careful examination of specimens. The pathological study is his.

† Read before the American Association of Pathologists and Bacteriologists at Washington, May, 1922.

to believe is not uncommon, and yet, as far as we are aware, is not widely known in this country. Its recognition thus far seems to have been confined to European observers. Its literature, strangely enough, covers but little more than the past decade, is almost entirely casuistic and concerned more with the clinical phases rather than the pathological. Even before this period descriptions of this lesion are by no means uncommon, but under the designation of "hyperplastic tuberculosis of the intestine" or syphilis. With a more rigid histological critique we believe this lesion can be partitioned from the large group of specific intestinal granulomata. Its interest is not entirely morphological. It is important clinically and is a malady which both the clinician and surgeon must consider in dealing with obscure tumors of the abdomen. The cause, with exceptional instances, is thus far unknown.

**Case Reports.** CASE I.—J. K., male, aged twenty-three years.

*Family History.* Father died of pneumonia; two sisters and one brother living and have always been well.

*Previous History.* The patient had measles, whooping cough, scarlet fever and pneumonia as a child. No rheumatism.

*Present History.* In December, 1917, the patient was first seen by one of us. He had a diarrhea averaging seven to eight movements a day for the past year. The stools were soft and occasionally tinged with blood; no cramps. He was a thin (112 pounds), pale somewhat anemic boy. There was a short presystolic murmur at the apex. The abdomen was lax, flat; no tenderness or mass. Under diet, etc., treatment and salol he improved so that he had but two or three fairly well formed movements a day. There was steady gain in weight (119 pounds). In May, 1918, he was operated upon for a typical attack of acute suppurative appendicitis from which he made a perfect recovery. In November, 1918, he had pain in the right iliac fossa. The bowels moved three or four times daily. A mass was found in the right iliac fossa, the size of a peach, firm, circumscribed and moderately tender. There was no fever. Weight has come down to 112 pounds. The condition remained practically stationary until February, 18, 1919, when he was operated upon by Dr. Wilensky. The cecum was found to be the seat of a hard firm mass. A resection was done with an end-to-side anastomosis. A fecal fistula persisted and remained open all summer. Bowels continued to move three or four times daily. In October, 1919, he was again operated upon by Dr. Wilensky. The fistula was closed. For the next year the bowels moved two or three times daily. Occasionally he would get attacks of diarrhea with more frequent movements, but without cramps. Such attacks usually lasted all night. In December, 1920, he suffered from an attack of acute intestinal obstruction. Resection of about a foot of ileum; the boy made a good recovery. The blood Wassermann was negative.

After this operation the patient felt well. His bowels moved two or three times daily, once or twice in the morning and once or twice after supper. There are no cramps with these movements. In January, 1922, he had an attack of six hours duration of abdominal pain, generalized and severe, with complete obstruction of the bowels. No vomiting, some fever. General impression, acute intestinal obstruction. Immediate laparotomy; large exudate of yellowish purulent material gathered for greater part on right side and under cover of great omentum and transverse colon; bowels distended; bowel well injected but not thickened and covered with fibrin in places. No local lesion was discovered to account for the peritonitis. Drainage was provided and the abdominal wall closed. A culture of the pus showed no pneumococci. The boy made an uneventful recovery.

FIG. 1.—Ascending colon, Case I, showing tumor constricting gut.

*Macroscopical Description. Colonic Specimen* (Fig. 1). The specimen consists of a piece of large gut 14 cm. long; the lumen of the middle half for a distance of 9 cm. is extremely constricted so that it is impossible for even the small finger to pass through. On opening the gut this constriction is found to be due to an extensive infiltrating swelling which begins imperceptibly at the proximal portion of the intestine so that the upper entrance to the structure is funnel shaped. The swelling becomes gradually thicker as one proceeds downward where it ends almost abruptly by a much thickened smooth and rounded ridge. The mucosa at each end appears perfectly normal; as it approached the thickening the folds become larger and smoother; on the summit the mucosa is almost per-

fectly smooth. The gut surrounding the strictured portion is tremendously thickened. On section through this portion the thickening involves all the layers: the mucosa, musculature and the mesenteric fat. The thickening is dense, hard and white. The external surface is comparatively smooth where it has been peeled away from the surrounding connective tissue. There are a few hemorrhages into the fatty layer.

*Microscopical Examination.* The mucosa shows a classical membranous inflammation. The superficial mucosa is congested and covered by a layer of varying thickness of fresh fibrin which springs from numerous crypts in the mucosa. In extensive areas the mucosa has been destroyed revealing ulcers covered by fresh fibrin beneath which the submucosal lymphatic tissue has been converted into frank granulation tissue. With the low power the entire thickness of the gut appears densely infiltrated. The cells are either heaped together in circumscribed clumps resembling the normal lymphoid structures of the intestine or scattered in lesser or greater densities throughout all the tissues. The clumps as well as the scattered infiltrations lie within the muscular zones causing extensive deformity of the muscle bundles. They are abundant in the fatty and connective tissues external to the muscular coat as well. With the higher power the infiltrating cells are those of the round- or plasma-cell type. In the more superficial tissues polymorphonuclear leukocytes are abundant, due to the contiguous acute membranous inflammation, but in the deeper tissues these are practically absent. A noteworthy finding is the presence of abundant giant cells. These are usually present within the solid lymphoid gland-like clumps of round cells described above. In some sections they are more abundant than in others and they are present in the deeper portion of the specimen as well as in the superficial. The giant cells are usually very large, oval or irregular in shape and connected with their immediate environment by numerous "pseudopodia." The giant cells contain numerous nuclei irregularly distributed. A rather strange finding is the presence of giant cells in what seems an apparently normal lymph follicle in a portion of contiguous colon that is otherwise entirely normal.

The vessels aside from containing abundant polymorphonuclear leukocytes in the superficial portions, show no change. Sections stained for tubercle bacilli and by Levaditi are negative.

*Macroscopical Appearance of Resected Small Intestine.* (Fig. 2) Specimen consists of a portion of small intestine about 8 inches long; with the exception of a small portion at each end, the gut is extremely thickened and enlarged. The peritoneal surface is much congested and is covered with fresh fibrin. Cross-section shows an immense thickening of all the coats of the gut so that the lumen is merely a bare slit. The infiltration involves the adjacent mesentery which averages 1 cm. in thickness; the villi are much

thickened and in consequence appear much wider and rounded than normal. The mucosa is deeply congested and the lumen contains a moderate quantity of fresh fibrin which covers the surface of the mucosa. Removal of the fibrin reveals numerous superficial flat ulcerations. The transition of the thickened portion of intestine into the normal is gradual.

*Microscopical Examination.* The microscopical appearance is practically identical with that of the preceding with one important and notable exception, namely, the presence of a far greater number of giant cells, the majority of which contain a peculiar foreign body. The giant cells are so abundant that on the average three or four are in every low power field. Many are still within the clumps of lymphoid-like tissues, but they now show an extremely

FIG. 2.—Cross-section of the small intestine, Case I, showing almost obliteration of the lumen by the granulomatous tissue.

irregular distribution. They lie imbedded within the muscular fibers surrounded with a sparse collection of round cells. Many are even in the subperitoneal connective tissue coat or in the mesenteric attachment. The giant cells (Fig. 3) are extremely irregular in size, usually round or oval in contour and have a scalloped border from which numerous pseudopodia connect it with the surrounding round cells. The nuclei are abundant and stain deeply. The nature of the containing foreign body cannot be distinctly made out, because morphologically the thing, even under oil immersion, has no definite structure or outline. As a rule it is round, sometimes oval, sometimes biscuit-shaped. It appears highly refractile and stains either not at all or pale with hematoxylon. Sometimes it appears coarsely lamellated; at others it consists of irregularly shaped refractile masses; sometimes a

giant cell, may enclose a simple faintly staining striated curved rod. In one or two the foreign body appears to have a radial arrangement. Whatever the masses may prove to be there is no question but that their structure is so dense as to have been injured by the microtome, because in the vast majority these foreign bodies apparently have been disrupted. It is for this reason that they lack definite structure. Sections stained for tubercle bacilli and by Levaditi are negative.

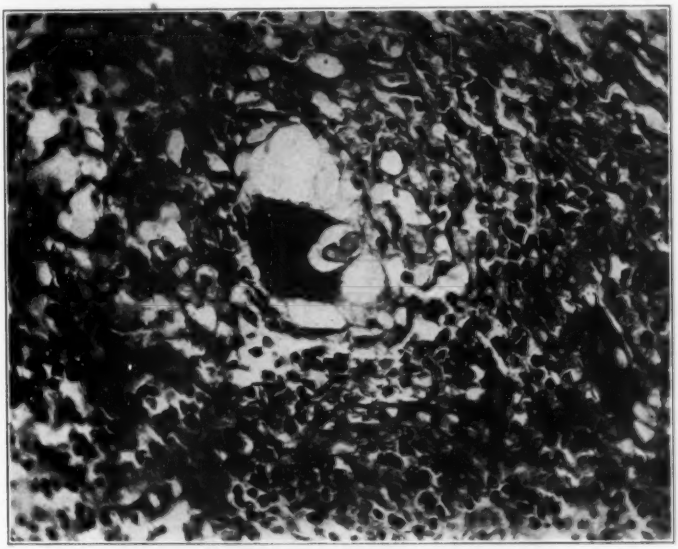

FIG. 3.—High-power of a giant cell, showing foreign body.

*Summary.* A man, aged twenty-three years, suffered from a diarrhea of a year's standing which responds to treatment. He is operated upon for an acute suppurative appendicitis. Six months later a mass in the right iliac fossa appears which is resected and proves to be a granuloma. He remains practically well for two years when an attack of acute intestinal obstruction occurs. At operation about a foot of ileum is resected. The gut is almost completely obstructed by a granulomatous growth extending throughout the length of the gut. Microscopically this growth is characterized by the presence of numerous giant cells surrounding foreign bodies of unknown nature. A year later an acute suppurative peritonitis occurs the origin of which could not be determined at operation. The patient at present suffers from a mild diarrhea, but is otherwise well. Every clinical and microscopical evidence of tuberculosis or syphilis is lacking.

Case II. (Obtained through the kindness of Dr. Seward Erdman.)—J. K., Russian, aged thirty-three years, operated upon at New York Hospital by Dr. Erdman in April, 1920, when he performed a resection of the cecum and ascending colon with lateral ileo-colic anastomosis. Eight days previous to admission he had suffered from pain in the right lower quadrant with vomiting and constipation. He denied having had any such symptoms previously. His appendix has been removed in the course of an

Fig. 4.—Ascending colon from Case II, showing stricture of the lumen by the granulomatous infiltration.

operation for right inguinal hernia in October, 1917, at the New York Hospital, at which time the operator (Dr. Vietor) remarked that the appendix was delivered into the wound with some difficulty and with some trauma to the cecum. The appendix did not appear to be diseased and it certainly was not indurated enough to interfere with the usual technic of invagination of the stump. In April, 1921, Dr. Erdman examined the patient and no masses in the abdomen were palpable. The patient said he felt perfectly well, had gained 20 pounds and was not suffering from any gastric or intestinal symptoms.

*Macroscopical Description.* (Fig. 4.) Specimen consists of a portion of large intestine 8.5 inches long. The opened bowel

reveals a raised tumor-like projection extending longitudinally at about its middle portion. The mass is situated on the posterior aspect, and measures 2 inches in the vertical diameter and 1.5 inches transversely at its widest portion and is three-quarters of an inch thick at its highest elevation. The mass is egg-shaped. The lower margin is thickened, curved with its convexity downward and overhanging. From here the mass narrows slowly as it courses upward and merges imperceptibly into the mucosa. Laterally the tumor overhangs the adjacent mucosa at its lower portion; above it merges gradually into the surface of the bowel. At about its middle, there is a flat ulceration with a slightly

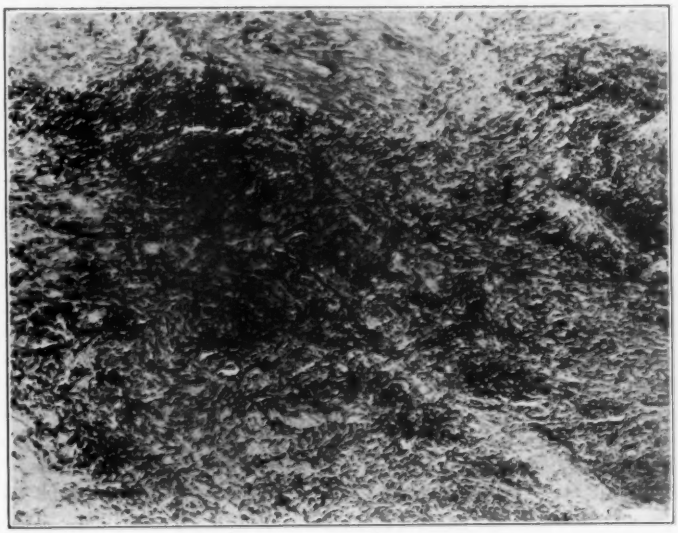

FIG. 5.—High-power section of colon, Case II, showing nature of the granulomatous infiltration.

roughened base, somewhat circular and measuring about 2 cm. in diameter. The surface otherwise is uneven, but the usual Kerckring folds are absent. Section through the mass shows a dense infiltration of all the coats of the intestine for a considerable distance beyond the confines of the mass.

*Microscopical Examination.* (Fig. 5.) Incidentally this section is representative of all the cases we present. The mucosa appears everywhere intact except at the site of the ulceration. Morphologically no abnormality is visible. The remaining coats of the gut are densely infiltrated with cells mostly of the round and plasma type. These cells are heaped together in dense but not

sharply circumscribed areas so that even grossly the cut section appears as though studded with tubercles. But there is a very great diffuse infiltration in all the tissues especially in the muscular layers so that the muscle bundles are separated, disorganized and deformed. The submucosa and subperitoneal connective tissue coats are much thickened due to an obvious fibroblastic transformation. These layers have all the appearance of young fibrous tissue. The lymphoid structures are intact and reveal nothing abnormal. The bloodvessels are numerous and show some thickening of the media. No giant cells are at all visible. In one section taken from the ulcerated area there is a circumscribed and apparently extensive infiltration with polymorphonuclear cells in the submucosa forming a small abscess. Lymph nodes removed from the mesentery are fairly large and are normal. Sections stained for tubercle bacilli and Spirocheta pallida are negative.

*Summary.* A man, aged thirty-three years, is operated upon for an inguinal hernia at which time an appendectomy is performed. Two and a half years later acute symptoms resembling those of an attack of appendicitis arise. A large mass in the ascending colon is found which proves on microscopical examination to be a simple chronic granuloma. The patient up to last reports is entirely well.

CASE III.—L. D., tool maker. Presbyterian Hospital (42738) (Path. No. 26199), admitted July 23, 1919. Five days previously had abdominal pain and vomiting. Appendectomy with drainage by Dr. Langworthy. Toward the end of convalescence the patient complained of pain in right upper quadrant and back. This persisted and is getting worse. Fever of 101° F. since onset.

*Physical Examination.* There is dulness in right upper quadrant extending to midline. Tenderness in this region extends back to spine. Recent healed appendectomy scar is visible. Stool and Wassermann were negative as well as the urine. No fever.

*Readmission.* April 24, 1921. Three weeks' complaint of general malaise, chilly sensation, pains in left lumbar region. The patient was told he had "nephritis;" later the physician diagnosed abscess around left kidney. Bowels were costive.

*Physical Examination.* In the left flank a mass is felt on bimanual examination, tender, smooth, firm, which can be pushed forward and backwards. No fever.

*Diagnosis.* Perinephritic abscess. Roentgen-ray shows a slightly enlarged left kidney, but no tumor of colon.

*Operation.* May 14, 1921, Dr. Auchincloss. Colectomy for mass just below splenic flexure.

*Macroscopical Description.* (Fig. 6.) The specimen is a segment of larger intestine, 21 cm. long. It is curved, forming the letter C about a central mass of tissue to which it is densely adherent.

This mass is composed of a rolled-up bunch of fat, the center of which is filled with innumerable whitish or reddish-yellow amorphous masses which suggest caseation but are not so soft. The colon is contracted, thick walled and contains fecal material. On section the colon appears normal, except in the distal edge of one segment of the gut where the tumor has encroached to the very edge of the mucosa but apparently has not broken through. The tumor at this point has been much narrowed.

FIG. 6.—Splenic flexure, Case III, showing granuloma of the mesentery infiltrating intestinal wall.

*Microscopical Examination.* Sections of the mesenteric mass shows a fibroblastic tissue containing many capillaries and densely infiltrated with round and plasma cells and leukocytes. The round cells predominate. In some places the cells are closely massed together which probably accounted for the yellow masses described in the gross. There is little actual necrosis of tissue. Section of one of the lymph glands on the outside of the mass shows a wide dilatation of the lymph sinuses with reticulum in which a few mononuclear cells are caught. Gram stain is negative. Section of the wall of the larger intestine shows a thin but intact mucosa with normal appearing glands and a slightly edematous stroma infiltrated with a few leukocytes and plasma cells. The muscular coat is edematous and densely infiltrated in many places with round cells. The submucosa is considerably thickened, quite vascular

and infiltrated with many polymorphonuclear leukocytes and a few round cells. Serosa covered with thin layer of fibrin.

*Diagnosis.* Chronic colitis, chronic mesenteric lymphadenitis. A blood Wassermann taken after discharge was negative. A fistula resulted which was closed by Dr. Auchincloss. The patient reported in November, 1921, as being perfectly well.

*Summary.* A man, aged forty-four years, is operated upon for an acute suppurative appendicitis. Appendectomy is performed. After the operation symptoms and signs suggestive of an inflammation in the right side of the abdomen appear which slowly subside. Nearly two years later he presents himself with a mass in the left kidney region which proves upon operation to be a granulomatous mass in the splenic flexure of the colon, the main bulk being in the mesentery but involving the walls of the gut and apparently not breaking into the mucosa. Miscroscopical examination reveals no evidences of tuberculosis, syphilis or lymphogranulomatosis. The patient up to last reports remains well.

CASE IV.—L. O., aged forty-four years, admitted to Presbyterian Hospital, December 26, 1918. (Presbyterian Hospital 40305 Path. Lab. 22256.) Three weeks ago she was seized with abdominal pains, cramp-like; vomited at onset. There was swelling of the abdomen, most marked in right upper quadrant, which went down considerably after a copious urination. Has had no severe pain since onset.

*Physical Examination.* In the right upper quadrant of the abdomen is a tender mass, extending to the upper epigastric region. It is round, smooth, somewhat movable and seems to descend on inspiration. This mass seems to be the lower pole of the kidney. Otherwise examination is negative. Wassermann is negative. Feces show no blood. Roentgen-ray shows a filling defect in the ascending colon just below the hepatic flexure.

*Operation.* January 18, 1919, Dr. Whipple. Colectomy and ileocolostomy. *Macroscopical Description.* The specimen consists of a cecum, appendix and a short portion of the ileum and ascending colon. The serosa of the cecum is smooth, the vessels are slightly dilated. There is a firm irregular nodular mass on the lateral aspect of the ascending colon, 13 cm. from the fundus of the cecum. The appendix is small, 3 by 0.3 cm. The lumen is obliterated. The cecum on section contains feces. The walls appear normal in thickness. The wall of the ascending colon is moderately thickened and the site of the dense mass described above. At one point there is a small nodule 1 by 3 cm. projecting into the lumen of the gut. Section through the larger mass shows a relatively dense tissue having a mottled yellow and white appearance. The gut wall is thickened at this point and the mass is adherent to it. Section through the small mass projecting into the lumen shows it to be

closely connected with the main tumor mass at a point in which the yellow substance described above is found in small areas in the gut wall extending as far as the mucosa.

*Microscopical Description.* All the coats of the intestine are densely infiltrated by a fibroblastic process which varies from a cellular and apparently fresh granulomatous tissue, with many newly-formed blood spaces to a comparatively dense fibrous structure. This new tissue is especially prominent in the submucosa and infiltrates the muscle to such an extent as to cause extensive separation and distortion of the bundles. The predominant cells are of the round type. These cells are heaped together in dense masses in many areas. There is no necrosis and no giant cells are found. The appendix shows complete obliteration of the lumen by fibrous tissue and extensive fibrosis of the muscular coats. The serosa is thickened and infiltrated with round and polymorphonuclear cells.

*Diagnosis.* Chronic colitis, chronic appendicitis.

Patient recovered and was discharged February 8, 1919. On July 17, 1919 she reported herself well.

*Summary.* A woman, aged forty-four years, is seized with sudden cramp-like pains in the right side of the abdomen. Upon admission three weeks later a large mass is noted in the right iliac fossa which proves upon roentgen-ray examination to involve the ascending colon. At operation, the mass is resected. Microscopically it proves to be a simple granuloma. The appendix reveals chronic inflammation. No microscopical evidences of tuberculosis, syphilis or lymphogranulomatosis are noted. Up to last reports the patient remains well.

According to criteria of pathology these 4 cases may be classified as "granulomata of non-specific morphology." All evidences of tuberculosis, syphilis, lymphogranulomatosis (Hodgkin's disease) or new growth are lacking.

**Gross Characteristics.** All 4 specimens with the exceptions of the small intestine (Case I) resemble one another closely. There is a firm dense uncircumscribed tumor involving all the coats of the large intestine causing stricture of the lumen. There is ulceration in all but 1 (Case III). The ulceration is comparatively superficial and does not penetrate beneath the mucosa. In 3 cases the ascending colon is involved, in the fourth the splenic flexure. The second specimen from the first case is the only one in which the small intestine is involved. It also involved all the coats of the intestine and the encroachment into the mucosa was so great as to cause almost complete obliteration of the lumen. Involving, as it does, almost a complete foot of the small intestine, the lesion, as far as we have been able to investigate, is unique. The infiltration was most prominent on the mucosal aspect of the

intestine in 3 cases. In the fourth, the main bulk of the tumor projected into the mesentery.

**Microscopical Characteristics.** The 5 specimens, again with the exception of the small intestine, reveal a uniformity in microscopical morphology. There is an extensive infiltration of all the coats with cells of the round- or plasma-cell type. It is hard to determine in which layer the infiltration is greatest, but to us the submucous layer seems most extensively involved. There is a widespread fibroblastic transformation varying from a comparatively richly cellular tissue to firm dense fibrous scar. The number of polymorphonuclear leukocytes in our specimens varies considerably. In those with ulceration they are numerous in the neighborhood of the ulcer. In the second case they are congregated in such abundance in the submucosa in one area as to justify the term abscess. In the remaining portions of our specimen these cells are only sparsely scattered. New bloodvessel formation is prominent in all specimens.

Giant cells are absent in all cases except the first. In both specimens from this case their distribution and morphology is so remarkable as to merit detailed description. In the first specimen removed from the ascending colon, the giant cells while easily found are not especially numerous, and are distributed equally throughout all coats of the intestine. They are large, have irregular dentated outlines and contain numerous nuclei irregularly distributed. They have none of the characteristics of either the giant cells of the Langhans type or the Reed-Sternberg type. A careful search reveals no evidence of foreign body in or contiguous to these cells. In the specimen of the small intestine removed from this patient, the giant cells are extremely numerous, three or four being present in almost every field. While morphologically they resemble the giant cells found in the colonic specimen, in these a foreign body is found within the majority of these cells. These foreign bodies have a varying morphology, usually they are round, oval or biscuit in shape, with a granular or highly refractile content and a dense lamellated capsule. What these foreign bodies are we have not been able to determine. They do not even afford the possibility of a guess.

In none of our specimens is there the slightest evidence of necrosis or caseation.

In Cases I and II, sections were stained for tubercle bacilli and the Spirocheta pallida but were not found. Bacterial stains on Cases III and IV were not made.

Sections of the mesenteric lymphatic glands reveal nothing noteworthy.

**Discussion.** It is a remarkable fact that non-specific inflammatory tumors of the intestine were, with few exceptions, not described until 1908. Practically the entire literature upon the

subject dates from the publication of Braun[1] in that year, and it is his report that has stimulated subsequent studies. It is true that in 1898, Graeser, in a classical paper, called attention to inflammatory processes in the sigmoid flexure arising from acquired diverticula, but such lesions, although morphologically similar to those in which we are interested, do not enter into our discussion. The reason of this curious absence of comment is the fact, as we shall discuss more fully in a subsequent part of this paper, that these cases were regarded as instances of "hyperplastic tuberculosis of the intestine."

Braun's case was that of a woman, aged forty-three years, who presented a tumor on the left side of the abdomen of eight weeks' duration. The bowels were irregular, often tinged with blood. Diagnosis, carcinoma. At operation a mass in the sigmoid flexure was found which involved mostly the mesenteric aspect. The mucosa covering the growth was normal. Microscopically the tumor consisted of a poorly cellular connective tissue infiltration of the meso-sigmoid which extended partly into the muscularis and the submucosa. In one portion there was a broad streak of round celled infiltration which penetrated to the mucosa.

The number of case reports since Braun's publication has been large and year by year shows a progressive increase, so that it is safe to say the malady is not at all a rare one.

We do not propose to submit a complete digest of all the literature pertaining to the subject. Those interested may refer to the fairly complete and most recent studies of Tietze[2] and Körte.[3] We shall merely content ourselves with giving a summary of the pathology, some of clinical aspects and the etiology.

PATHOLOGY. Each of our cases exemplifies in one way or another the characteristics common to this lesion. There is a tumor of greater or lesser size which many involve any portion of the colon. Even in the sigmoid many such lesions are described without in anyway being associated with a diverticulitis. The inflammatory process usually involves all the coats of the intestine. Sometimes the proliferation is most prominent in the inner coats forming smaller or larger tumors which narrow the lumen of the gut. Less frequently the proliferation seems to begin in the mesenteric attachment forming tumors sometimes even as large as a child's head, which involve the walls of the gut by continuity and cause stricture of the lumen. In the former, there is ulceration of the mucosa, which, as a rule, is superficial and not extensive; in the latter the mucosa appears perfectly normal or slightly thickened. Adhesions to surrounding structures and to the abdominal wall are common. In a few instances, the induration has extended to the ileo-cecal valve causing narrowing of this structure. Abscess formation is rare, and when present is slight as in one of our cases.

MICROSCOPICALLY. These tumors reveal typical granulomatous changes in various stages of senescence and the descriptions we have submitted in reporting our cases (excepting Case I which is almost unique) cover the ground quite fully. There is never the slightest evidence of tuberculosis, syphilis, lymphogranulomatosis or new growth.

The remarkable resemblance of some of the cases which we report to hyperplastic tuberculosis of the intestine led us to a study of the literature of this malady in order to check up our findings. We have arrived at the conclusion that undoubtedly many if not a majority of so-called "hyperplastic tuberculosis of the colon" are really simple granulomata. Indeed the majority of authors of comprehensive papers on "hyperplastic tuberculosis of the intestine" describe lesions that are identical in every way to those which we have reported. For instance Lartigau[4] says, "More often the tubercles are mere aggregations of lymphoid cells in which one or more giant cells are seen. Epithelioid cells are usually absent. Many show little tendency to necrotic change; a distinct tendency to fibrous transformation is apparent. *The typical histological features of tubercle bacilli are often absent;* in lieu thereof there may exist a diffuse embryonal cell differentiation, at times capable of simulating sarcoma." Ignard[5] says, "In many cases of hyperplastic tuberculosis of the intestine, no tubercles, giant cells or bacilli are found. The lesion is constituted of a mixture of variable proportions of tuberculous and inflammatory elements. *In certain cases, the last only exist.* Nevertheless, these inflammatory tumors should be classified among the tuberculous." Itie[6] says, "The tuberculous elements are relatively rare. More often you find simple follicles with two or three giant cells. The zone of epitheloid cells is wanting, and only a crown of round cells surrounding a giant cell is found." Pilliet and Hartman[7] say that "Hyperplastic intestinal tuberculosis differs from the common tubercle. The tuberculous follicles are relatively rare; the embryonic infiltration on the other hand is more marked." Weiting[8] after calling attention to the fact, "That tuberculosis may cause an immense amount of connective tissue infiltration without any tendency to break down," remarks in a late portion of his paper, "that a diagnosis of tuberculosis must be excluded unless tubercles with giant cells are present." Shiota[9] who describes 24 cases of so-called hyperplastic tuberculosis remarks, "That it is common not to be able to differentiate the lesion from an inflammatory hyperplasia." Ipsen[10] says, "That tuberculosis may be present even though the characteristic histological reaction is absent, and that the diagnosis can only be confirmed by animal inoculation." Incidentally, as regards intestinal tuberculosis, we have been unable to find in the literature that this procedure has

been performed. He regards "a late invasion by the organism as a possible explanation for the absence of the characteristic histological characters." Doubt seems to have crept into the mind of but one observer, Richter.[11] He believes that hyperplastic tuberculosis is really a non-specific inflammation of the cecum and that the tuberculosis is only an accidental infection and complication, the result of swallowing tubercle bacilli either from a pulmonary focus or in milk.

It does not require much reading of studies of intestinal tuberculosis to discover that observers have copied each other's discussions closely. For instance, nearly all try to account for the non-tuberculous characteristics of their lesions by likening them to lupus. It remained for Richter to disclose the fallacy of this assumption. Furthermore, all comment on the sparseness, or what is more significant, the absence of tubercle bacilli in such tissues, although only very few mention any attempts at finding them in the lesions they report. At all events, the scarcity of bacilli is supposed to account for the absence of the typical histological characters of tuberculosis in these lesions, but on what grounds we do not know. Tubercle bacilli are scarce in many frankly tuberculous lesions, but nevertheless, the lesions are unmistakable. The absence of bacilli in the lesions they describe is certainly significant, but this seems to have escaped notice.

We believe, therefore, with more rigid methods of histological study, the number of true hyperplastic tuberculoses of the intestine will diminish appreciably and that in the future fewer will be reported than heretofore.

The criticism we have submitted also accounts in a large measure for the comparative absence of reports of non-specific granulomata of the intestine up to the year of Braun's publication.

Etiology and Pathogenesis. In the vast majority of the reported cases the etiology was unknown. A curious feature in all 4 cases which we report is the history of a previous appendicitis or appendectomy. In 2 cases (I and III) a definite acute suppurative appendicitis preceded the onset of signs six months and two years respectively. In Case II an appendectomy in the course of herniotomy was performed three years previously. (Whether the appendix was diseased or not can no longer be determined.) In Case IV the history suggested an acute appendicitis three weeks previous to the onset and pathological examination of the appendix revealed a completely obliterated organ.

The relationship of inflammatory lesions of the colon to appendicitis is repeatedly broached in reported studies. (De Ruyter,[12] Gangitano,[13] Läwen,[14] Gato,[15] Teitze,[2] Körte.[3]) In most of these reports however, the inflammatory process is continuous with that of the appendix and involves only the contiguous portion of the

cecum. In other instances mere coproliths are present or old obliterations at the tip. Despite the frequent associations of inflammatory lesions in the colon and appendicitis, we are forced to the conclusion, taking into consideration all possible genetic factors, that this relationship is entirely coincidental. We cannot conceive how a chronic granuloma in the colon can arise at a distance from an inflammed appendix removed six months or two years previously or an appendectomy performed three years before the onset of signs. Even if such a late infection were possible, it could only arise by way of the lymphatics, and while it is true according to Bartels[16] that the lymphatics of the appendix and cecum anastomose, the current is in the reversed direction. To assume that an infection occurs in the retrograde direction would be stretching possibilities unduly. Another possibility is that the presence of a dormant infection in the gut contributed to an infection of the appendix. There is little question, judging from the morphological characters, that the granuloma was present in the gut long before clinical manifestations became apparent and it is conceivable that such a mass, probably already ulcerated, would render an infection of the appendix more liable. In this connection it is interesting to note that a primary typhlitis of the cecum, a lesion resembling those which we describe very closely has been reported occasionally, in many instances such a lesion being regarded as the course of a subsequent appendicitis. For many years the occurrence of a primary typhilitis was doubted but it unquestionably occurs. Haim[17] reports many such.

There are a number of case reports of granuloma of the colon in which foreign bodies were the direct cause. Jaffe[18] found a tumor the size of a fist involving the colon in the center of which a small piece of bone was found. Schreiber[19] reports a large ulcerating granuloma of the ileo-cecal region in which many cherry and plum pits were present. Marion[20] reports a piece of bone in a large granuloma of the ascending colon adherent to and involving the rectus muscle. Tietze[2] reports a granuloma in the cecum following an operation for acute appendicitis. In the center of the granuloma the silk thread employed in ligating the appendix was found. Wölfler and Lieblein[21] in their comprehensive monograph on "foreign bodies in the intestine" remark on the frequency of lodgement of such bodies in the cecum where they give rise to large inflammatory thickening with adhesions and occasionally to perforation with chronic abscess formation.

The only specimen in our series in which a foreign body was present is Case I in which microscopical foreign bodies of unknown structure were found enclosed within giant cells. What the nature of these structures are is unknown to us. These foreign bodies we believe penetrated into the wall of the gut through previous

ulceration consequent to colitis. No foreign bodies were found in the other specimens, either on section or by roentgen-ray.

A colitis or dysentery has been reported as preceding the onset of these granulomata by numerous writers, (Monsarrat[22], Rosenheim,[23] Strauss,[24] Birt and Fisher,[25] Koch,[26] Gato[15] and Tietze[2]). In our first case a colitis was probably the origin of the granuloma, if a long standing diarrhea with blood and mucus in the stool is at all diagnostic of a colitis. Tietze reports a case of inflammatory tumor of the sigmoid flexure following irrigation of the lower bowel with a strong silver nitrate solution.

The derivation of granulomata from diverticulitis of the sigmoid is well known. This malady, however does not enter into our discussion.

In the vast majority of instances the cause of the granuloma is unknown. We must presume that there is some infectious agent of low grade violence which enters through the mucosa. Distribution of the infection by lymphatics is in most instances highly probable. The lesions remind one strongly of the granulomata described by Braun[27] and others which occur in the omentum following ligation and resection of this structure in herniotomies and which are due to infections from silk or catgut. Rarely, these granulomata arise from infections in the stomach, Fallopian tubes or ovaries. They also resemble the inflammatory tumors of the abdominal wall described by Schloffer,[28] arising after operations for hernia, in which silk stitches are occasionally found imbedded within the tumor.

Clinical Considerations. A survey of our report readily leads to the deduction that the lesion we report offers no characteristic clinical concept: the etiology, symptoms and signs are too protean and indefinable. Evidence of a stenosis of the gut and the presence of a mass in the abdomen are by all odds the most constant phenomena. The most prevalent diagnoses have been malignant growth, hyperplastic tuberculosis and appendicitis and most observers agree that a correct preoperative diagnosis is impossible. The most interesting and diagnosticable characteristic in connection with these granulomata of the intestine is their disappearance after a simple sidetracking operation. Moynihan[29] and Robson[30] report such instances. Obviously the presence of a tumor of this variety has a profound bearing on prognosis.

**Conclusions.** 1. Four cases of non-specific granulomata of the intestine are described. All involved the colon, 1 involved both colon and small intestine.

2. The histological characteristics are those of a simple granuloma. No evidences of tuberculosis, syphilis or lymphogranulomatosis are present.

3. The granulomata may involve any portion of the colon.

The infiltration of the wall may be more prominent on the mucosal or the mesenteric aspect. In both instances the lumen is narrowed. Ulcerations, which are usually superficial, may be present; exceptionally, abscess formation.

4. The cause most often is unknown. In a few cases foreign bodies and a colitis have been reported. Despite the association of the lesion with a previous appendiceal involvement we do not believe that appendicitis has any direct causal relationship to the malady.

5. Clinically, these cases present signs of constriction of the intestinal lumen and a mass in some portion of the colon. Thus far, they are not diagnosticable before operation and have usually been mistaken for carcinoma and tuberculosis of the intestine. Not infrequently these tumors disappear after simple sidetracking of the intestine. The prognosis is excellent.†

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# THE ROLE OF SPASTICITY IN DISEASES OF THE DIGESTIVE TRACT.*

## A Case of Visceral Tetany, Causing Acute Cholangitis and Pancreatitis.

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It is the object of this paper to contribute to a better understanding of the role which spasticity may play in diseases of the digestive tract.

The knowledge of abdominal spasticity is not new. The writings of older clinicians show that they were familiar with the phenomenon. Roentgenology however, demonstrated its great frequency and taught us to differentiate more sharply its various forms and types and their relation to tonus, peristalsis and segmentation (hypermotility, hyperperistalsis, tonic and tetanic contractions). Granted that the appearance of spasticity has generally been recognized, its interpretation and valuation is often far from satisfactory.

Its frequent occurrence with local conditions, such as traumatic lesions, stones, acute inflammations, ulcerations and cancer, led to the more common explanation of spasticity as a manifestation of localized character, a plausible explanation on account of the automatic activity of the ganglia implanted in the digestive tube. And yet operative, as well as postmortem inspection, found the lesion often at a different spot than the location of the spasm would indicate. Ulcer or cancer at the cardia with spastic obstruction in the upper part of the esophagus; ulcer or cancer at the smaller curvature with pronounced spasm of the uninvolved cardia; gall stones and cholecystitis associated with true gastrospasm or with tonic contractions in the colon and sigmoid. The spasm in parts distant from the lesion is produced reflexly over the paths of the vegetative nerves which regulate the coöperation of the different sections of the digestive tube. Reflex spasm may also originate from organic lesions outside the alimentary canal, from diseases in the central nervous system, the pelvic and other organs. These two types, local and reflex spasm, will not be further discussed here since they predominate in the interpretation of spasticity at present. I rather intend to emphasize a fact too often overlooked, that spasticity, eventually of a very high degree, may, as the result of systemic derangements occur without the presence of a local lesion.

* Read at the Twenty-fifth Annual Meeting of the American Gastroenterological Association at Washington, D. C., May 1, 1922.

AUTONOMOUS SPASTICITY. The conception has been entertained long ago that spasticity may present itself as part manifestation of conditions which we are still accustomed to class as general neuroses.

In his classic essay on "Peristaltic Unrest" Kussmaul[1] attributed the painful and visible hyperperistalsis of the stomach and the bowels, to a highly increased irritability of the peristaltic nerves in neurotic individuals, at the same time stating with regret that the term motor neurosis did not convey much meaning. Under his influence Fleiner[2] defined spastic constipation.

The modern study of the working of the vegetative nerves, greatly stimulated since the description of vagotony by Eppinger and Hess,[3] has considerably advanced the understanding of spasticity of systemic origin.

We have learned that normal activity of the digestive apparatus requires a harmonious interplay of the vagus and the sympathetic and that it depends on a maintenance of steady tonus in the two systems. However, the habitual tonus of the vegetative nerves varies greatly as to degree in different individuals, and even in the same person it varies at different times according to his constitutional make-up. Constitution has been aptly defined as a person's characteristic way of reacting to internal and external stimuli. Coined on this basis, the term "spastic constitution" is suggestive. Such definitions make it easier to comprehend that the same type of local lesion may provoke frequent and severe spasm in one person, and rarer and milder spasm in another; and further, that a local lesion may exist without causing spasm, that for instance, stones in a gall-bladder may remain dormant, often for a long period of time, until something occurs in the system which provokes spasm in the biliary ducts and with it "an attack." Even the structural narrowing caused by cancer often becomes evident only at a time when spasm is superimposed and produces the symptom-complex of obstruction. Persons with habitually high irritability of the vegetative nerves seem to be disposed to a further increase of tonicity by anything affecting their physical and mental balance, foremost of all by fatigue after physical, mental, or emotional taxation.

Once we have reached this viewpoint, the association of local lesions with spasticity may appear in a different light. While in certain conditions the local lesion must be held chiefly responsible for bringing on the spasm, for other conditions the question may well be asked whether the spasm is not primarily the result of systemic influences, and instead of being an effect, is not, in fact, a causative element in the development of the lesion.

[1] Samml. klin. Vortr., 1880, No. 181, p. 1638.
[2] Berl. klin. Wchnschr., 1893, **30**, 60.
[3] Die Vagotonie, Berlin, 1910.

Spasticity as a Causative Factor. The valuation of spasticity as a causative factor has been extensively dwelt upon in the discussion on the pathogenesis of peptic ulcer. Experimental investigators, pathologists and clinicians join in the contention that the primary lesion, that is, the miliary ecchymoses, are caused by spasm of the muscularis mucosæ which constricts the small end-arteries and leads to ischemia and extravasation. When a strong peptic secretion is present, which like the muscular spasm is the result of excessive vagus tone, the poorly nourished part of the mucosa in the area of ecchymoses is digested, and we have an erosion. The development of an erosion into an ulcer and its further growth are possible, however, only when there is more than temporary overirritation of the vagus nerve. It requires a distinct disposition, which manifests itself by a chronic state of increased vagus tone, bringing on prolonged periods of hypersecretion and spasm not only of the muscularis mucosæ, but also of the larger muscular coat and eventually of the pyloric sphincter. The regular recurrence of spasm with each meal prevents the healing of the ulcer and makes for its chronicity. Once developed, the ulcer as a source of irritation may further increase the vagus tone thus creating a vicious circle. From the very start and through the whole course of the ulcerative process we see spasticity as an important causative element.

If we accept these views which offer a plausible theory of the mechanism in the development of certain types of peptic ulcer, we still have to answer the question: What causes the spasticity or rather the excessive vagus tone, which is at the bottom of the ulcerative process? At present the opinion prevails that it is provoked reflexly by a local lesion somewhere else in the system, especially by a diseased appendix, in short that peptic ulcer is a "secondary disease" (Rössle).[4] I am not ready to subscribe to this opinion, having seen too many cases where the ulcerative process recurred or even started only after the removal of the appendix, and also hesitate on account of similar experiences after other operations. On the contrary, I think clinical observations justify the contention that increased irritability of the vagus with consequent spasm may be produced directly by the action of systemic influences, (diets, etc.) metabolic disorders, autointoxication, lead or tobacco poisoning and other factors. As I pointed out four years ago,[5] mental and emotional overtaxation, probably by way of disordered endocrine influences, may be the principal causative element in the development of excessive vagus tone, spasticity and active periods of ulceration. Only when we realize the importance of systemic factors are we able to explain the well known periodicity of peptic ulcer. This periodicity is but a con-

[4] Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1912, **25**, 766.
[5] Med. Record, 1918, **94**, 324.

firmation of the axiom, that disease is not static, but a functional disorder with stages of development. The local reaction is merely a manifestation in a certain region of predisposing systemic agencies.

It is this point which I wish to stress, that spasticity resulting from systemic conditions may be a primary causative factor in peptic ulcer, and in a similar manner in other local lesions in the digestive tract. There is at present too much inclination to look for a direct causal relation between the different diseases in the stomach, intestines and gall-bladder, making one the provocative agent of the other. It is certainly true that, for instance, a diseased appendix may reflexly cause disorders of the gastric function. Such possibilities, however, are far too often generalized. It occurs to me that we may arrive at another view by investigating, whether each one of simultaneous but different local lesions met with in the same person, was not originally the outcome of a systemic disorder. This view would rather tend to coördinate them, and would minimize the influence, which after their initial development they may have had upon each other.

Without entering now upon a discussion of the nature of the underlying general condition, I repeat that spasticity caused by systemic upsets, may prove an important factor here. By approaching these problems in a changed mental attitude, clinical syndromes may assume to the observer a different significance.

Since abdominal surgery demonstrated the frequency of acute infections especially in the appendix and gall-bladder, conceptions of abdominal pathology have been strongly influenced by the picture of inflammation. The result was that not only in acute, but likewise in chronic conditions, objective as well as subjective symptoms, such as tenderness and pain, were too readily accepted as signs of inflammation. This, for instance, is clearly seen in the poorly defined syndrome of "chronic appendicitis," the diagnosis of which is principally based on the evidence of spontaneous and pressure pain in the appendicular region. The fact that in a high percentage of cases thus diagnosed as chronic appendicitis, the same spontaneous and pressure pains recur after appendectomy, proves that the pain did not originate in the removed appendix. When not caused by another local lesion or not of a purely neuralgic character, the pain in many of these cases is the result of uncomplicated enterospasm. We do well to keep in mind, that in the digestive tube, as elsewhere, spasm by itself may produce pain, eventually of severe character and of long duration.

For a while the idea of the existence of true nervous gastrospasm and of enterospasm was actually ridiculed; it has come into its own again since the roentgen-ray visualized such spasms. It is significant that a surgeon, Liek[6] in Danzig, after a thorough

[6] Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1921, **32**, 153.

study of the literature and of his own vast material, rejects the popular syndrome called chronic appendicitis. He adopts instead the term pseudo-appendicitis, attributing the pain in most of these cases to nervous enterospasm.

When the spasm is localized at the appendix, it may cause stasis, bacterial growth and inflammation. In such an event inflammation follows the spasm. Acute appendicitis is frequently preceded by attacks of "appendicular colic" without fever and without changes in the blood picture.

A similar situation may arise in the biliary tract. In a paper[7] read before this association nearly twenty years ago, I stated that spasm at the opening of the common duct, by causing biliary stasis, may lead to the formation of gallstones, to calculus attacks and to infections and inflammations of the bile ducts and of the gall-bladder. Gerster[8] independently arrived at similar conclusions in a paper in which he dealt with the causes of unsuccessful surgery in disorders of the gall ducts. And Meltzer[9] discussed this topic thoroughly at a symposium on diseases of the gall-bladder in 1916. That the same underlying condition of autonomous spasticity should create such entirely different products as a clean-cut peptic ulcer or a purulent inflammation is not so strange if we consider the different character of the respective secretions, especially the peculiar qualities of the gastric secretion, which not only digests poorly nourished parts of the gastroduodenal wall but also destroys bacteria.

Clinical experiences over a course of years have convinced me that spasm alone, due to systemic upsets, more frequently than is generally conceded may account for severe abdominal pain; furthermore that it may become the primary causative factor in the development of abdominal diseases including local inflammations. As an illustration I present the history of a patient, whom I had occasion to observe together with his physician (Dr. A. L. Garbat) and with other consultants.

**Case History.** L. M., male, aged fifty-five years, grew up under trying circumstances. From childhood on had to do very hard work, while for many years he was provided with poor food. At an early age dental decay set in and was neglected, so that eight years ago, all teeth had to be extracted. From early days whenever his stomach was upset frequent and long attacks of hiccoughs appeared. He always had a tendency to "indigestion" with heartburn and sour eructations. Appetite was usually good, bowels were constipated.

[7] Kaufmann, J.: Am. Med., November, 1903, **6**, 792.
[8] Surg., Gynec. and Obst., 1912, **15**, 572.
[9] Tr. Am. Gastroenterol. Assn., 1916, p. 116; Am. Jour. Med. Sci., 1917, **63**, 469.

No acute attacks of pain ever occurred until the present trouble.

In 1906, at the age of thirty-four, pleurisy with effusion was contracted. Was tapped twice with removal of 92 oz. of fluid. Tubercle bacilli were present in the sputum. Involvement of left upper lobe and right apex were found. After prolonged stay and treatment at Saranac, New York, was discharged with general improvement and gain of weight. No signs of an active process showed themselves until 1913, when an attack of fever and cough required his return to Saranac. After this the picture remained that of an inactive, stationary fibrosis of the left upper lobe and of the right apex. Patient returned regularly to Saranac during the summer months, and several times during the year for a few weeks, whenever he felt run down. On these occasions more cough and more sputum were noted with tubercle bacilli. During the rest of the year, the high strung, energetic, short and moderately nourished man worked steadily and over long hours as boss of a barber-shop in a big hotel, where he had "to handle from 600 to 700 customers a day."

In the summer of 1920, while at Saranac, the first attack of severe epigastric pain set in. It penetrated to the back, was taken for an acute indigestion, although the possibility of gall stones was also considered. The second attack came on June 5, 1921. Severe pain on right side, the entire right side was rigid and very tender, so that it was difficult to differentiate between gall-bladder and appendix. Temperature up to 103°; while white cell blood count was 12,000, 84 per cent polynuclears, 16 per cent lymphocytes. Light jaundice. Fever and tenderness gradually disappearing. While in bed for about three weeks undergoing a modified "Carlsbad cure" with application of heat to the right upper side, a sudden attack of very severe pain on the left side set in, radiating into the scrotum and left thigh, bearing all the earmarks of a renal colic. No red blood cells or concrements were found in the urine. He was greatly benefited by the Carlsbad treatment, and went to the mountains for the whole summer and remained free of pain until September, 1921, when renewed attacks of very severe pain in the upper abdomen set in, radiating to the middle of the back and to the right shoulder. They became more frequent, finally occurring every day. The pain was usually of such a severe character that no medication except morphin hypodermically would give relief. At no time were fever or jaundice present. The roentgen-ray showed stones in the gall-bladder.

October 5, 1921, Dr. John Erdman removed the gall-bladder with 77 stones and 5 stones from the common duct. The gall-bladder was thickened, firmly adherent to the liver and to the surrounding tissues and was separated with great difficulty. No signs of acute inflammation were found. Cultures from the gall-

bladder were sterile. Free flow of bile was secured by drainage. Uneventful recovery until the twelfth day after the operation (one day after removal of the drainage tube from the bile duct) when the patient suffered again an attack of very severe abdominal pain of the same character as before. A week later he had a similar attack. From then on the attacks occurred more frequently, finally every day and even two or three times within twenty-four hours. The pain, excruciatingly severe, varied in its location. At times it was felt in the middle of the abdomen, radiating toward the back or the chest and in the latter event causing severe dyspnea; at other times it would start in the right upper side radiating toward the groin. Not infrequently the paroxysm was preceded by painful peristalsis and gaseous borborygmi. On several occasions, particularly with the onset of phosphaturia (see further below) very severe pain occurred on the left side, shooting into the bladder. It was associated either with great difficulty to pass urine, or with very frequent voiding of small quantities of urine. This dysuria was observed at other times with clear urine.

The paroxysms came on at irregular intervals, at any time during the day or the night. They were not in any way related to meals, were occasionally alleviated by an enema and alvine evacuation, and were, as a rule of such a severity, that none of the many drugs tried would give relief except morphin hypodermically administered.

With numerous attacks occurring over a period of about four months no fever or any other signs of inflammation were ever observed.

The blood picture was that of secondary anemia. On January 12, 1922, the hemoglobin was 75 per cent, red blood cells 4,368,000; leukocytes 7200; polymorphonuclears 73 per cent; lymphocytes 27 per cent. Wassermann negative.

The blood pressure was low, systolic 90 to 100, diastolic 40. No disorders of the heart.

Fluoroscopic combined with serial roentgenographic examination of the gall-bladder region, stomach and duodenum done on November 21, 1921, did not reveal any evidence of stones in the biliary ducts. The report of the roentgenologist continues as follows:

"We gave the patient the usual barium meal, and examined him in all different positions, both erect and prone. We were at once struck by the very vigorous hyperperistalsis, marked writhing contractions were seen almost immediately and continued through the entire observation. On manipulation under the screen, we found evidence of adhesions binding down the prepyloric region of the stomach and the first portion of the duodenum. On the upper border of the bulbus there is a persistent defect.

"In postoperative cases, one has great difficulty in deciding what is producing such a deformity to the outline of the first portion of the duodenum. It must be either one of two things, adhesions or true ulceration. Considering the character of the shadows, the persistency of the deformity, and the fact that we had such very marked hyperperistalsis, it would seem to be some ulceration."

After an examination of the entire urinary tract on December 13 the report reads:

"I fail to find any evidence of nephrolithiasis, nor do we find any shadows that are even suspicious of a stone in either ureter. In the bladder, well down toward the symphysis, we see some irregular shadows which suggest calcareous deposits in close relation to the prostate.

"The left kidney seems somewhat enlarged but is normal in size and position. The right kidney is not clearly outlined owing to the presence of gas and fecal matter in the proximal colon.

"If you will refer to my report of Mr. M's examination of November 21, you will note that I referred especially to the presence of a very vigerous hyperperistalsis. I also reported a distinct deformity to the first portion of the duodenum and in my conclusion stated that I believed the man had a duodenal ulcer."

Gastric analysis after test-breakfast showed nothing abnormal: free acid, 36; total acidity, 58.

Stool as a rule very scanty, dry hard scybala, often passed only with great difficulty, denoting spastic constipation. At other times the stool was copious, mushy, acid, reminding one of a pancreatic stool, without, however, showing impaired digestion of fat, starches or meat. No occult blood in feces.

Duodenal drainage on January 27, 1922; tube inserted at night; next morning with fasting stomach after application of 50 cc of 20 per cent magnesium sulphate solution, immediate free flow of bile. First portion dark and thick (absence of gall-bladder); during the following six hours about 500 cc of bile were gained, light yellow, viscid, without sediment, showing on microscopical examination neither leukocytes or epithelial cells, nor crystals. Culture sterile.

Whenever I had occasion to see the patient, I was impressed by a marked tendency to spastic conditions. At various examinations abdominal muscles between the attacks were found contracted and rigid; during attacks the whole abdominal wall appeared board-like in tetanic contraction. Having his attention aroused, patient reported, that at this period during meals, he frequently had to drop fork or knife on account of cramps in his hands. When walking he often had to stop for a while to let pass severe cramps in calves or feet. Even when in bed the abdominal paroxysm was frequently preceded or followed by cramps in calves or feet, often of very great severity. At one time (middle of January, 1922), he felt severe pains in the little fingers and in the big toes. I have already mentioned the spastic bladder condition.

This impression of spasmophilia was strengthened by findings of disordered calcium metabolism. While the urine as a rule showed nothing abnormal, during the month of December, 1921, for several weeks regularly, and in January, 1922, for a while intermittently, the urine was of peculiar and unusual character; freshly passed, the urine was turbid, strongly alkaline, had a very pungent odor of ammonia and a very heavy whitish powdery sediment, which the microscope revealed as consisting partly of amorphous material, to a greater extent, however, of triple phosphate crystals, while there were no cellular elements pointing to an inflammation of the urinary tract, and no indication of bacterial fermentation.[10]

At a time when the urine had been clear for a while, a study of the calcium metabolism by Dr. A. Bernhard, pathological chemist to the Lenox Hill Hospital, showed the following:

TABLE I.—METABOLIC STUDY OF CALCIUM.

| | Total quantity. | Calcium as CaO. |
|---|---|---|
| January 20 to January 21, 1922: | | |
| Excretion: | | |
| Urine | 1000 cc. | 0.335 gm. |
| Stool | 256 gm. | 3.910 " |
| Total | | 4.245 gm. |
| Intake (milk diet) | | 3.900 gm. |
| Loss of calcium during first day | | 0.345 gm. |
| January 21 to January 22, 1922: | | |
| Excretion: | | |
| Urine | 1450 cc | 0.529 gm. |
| Stool | 249 gm. | 8.510 " |
| Total | | 9.039 gm. |
| Intake (milk diet) | | 2.500 " |
| Loss of calcium during second day | | 6.539 gm. |
| Average daily calcium excretion in urine[11] for two days | | 0.432 gm. |
| Average daily calcium excretion in feces[12] for two days | | 6.210 " |

*Chemical Examination of Blood.* Urea nitrogen, 22 per cent; creatine, 1 per cent; uric acid, 5 per cent; sugar 0.08 per cent; calcium, 6.2 per cent; (normal calcium, 5.3 to 6.8 per cent.)

From a report of the status of the nervous system taken on January 21, 1922, I quote the following:

Pupils equal, both react to light, accommodation and consensually. There is no disorder in the territory of the facial nerve. The tongue is coated, but protrudes in the median line, and shows

[10] Regarding the relation of phosphaturia to disordered calcium metabolism, I refer to F. Umber (Ernährungs- und Stoffwechselkrankheiten, Ed. 2, 1914; chapter on Phosphaturia, p. 469).

[11] Normal excretion of Ca in urine 0.1 to 0.4 gm.

[12] Calcium elimination by feces normally between 60 to 90 per cent of the amount ingested, while in this case, with only 6.4 gm. intake, there was an excretion of 12.42 gm. instead of 5.7 gm. at the utmost.

no atrophy or fibrillation. No motor disorder manifest in the entire body; no sensory disturbance except as indicated below. Deep reflexes markedly increased; superficial reflexes are normal except for an absence of the upper and lower abdominal reflex on both sides. Some hypalgesia over the left lower abdominal region. Mechanical excitability of the muscles of both forearms, markedly increased with a pronounced idiomuscular ridge easily produced. Mechanical excitability of right lower abdominal muscles markedly increased. Electrical reactions normal except in the muscles of the right lower abdominal region (scar territory) in which there is a reduced faradic excitability and anodal closure contractions greater than cathodal closure contractions, in the abdominal muscles due to the incision made in the right lower abdominal region.

Although this examination showed no electrical hyperexcitability of the peripheral nerves at the time of the examination, the various manifestations of tetanoid contractions of peripheral muscles before and after this examination suggested the probability that we were dealing here with a similar hyperexcitability of the abdominal vegetative nerves with consequent spasm and pain, as were indicated by the finding of intense gastric hyperperistalsis during the roentgenological examinations. Attempts to correct this condition by dietetic and various medical treatments, including the administration of parathyroid and calcium chloride by mouth, proved futile, so that, when at the end of January the paroxysms of pain became more frequent and for several days required two, to three morphin injections within twenty-four hours, we decided to open the abdominal cavity once more, considering the possibility that a remaining gall stone, cancer, or another undiagnosed local lesion might be the provocative agent. At the wish of the patient the operation was set for a certain date, when a complete change of the picture necessitated an earlier operative interference. On February 2, with an atrocious attack of pain particularly severe in the back, fever up to 102° and pronounced jaundice were observed; the urine was full of bile, the stool clay-colored (careful searching of the stool for a number of days failing to find stones).

Operation. February 3, 1922. Dr. John Erdman found dense adhesions at the site of the removed gall-bladder impinging upon the common duct. The common duct was readily exposed and found fairly dilated. Upon opening the common duct, a considerable amount of purulent material was extruded, a scoop and catheter, the latter the size of number sixteen French readily passed through into the duodenum. No stones in common or hepatic ducts; no signs of peptic ulcer. Head of pancreas considerably swollen and indurated; choledochostomy was completed by sewing the catheter into the duct and drainage established. Culture of common duct content showed pure cultures of B. coli communis.

For two days an uneventful course, except for frequent vomiting. From the third day on the spastic tendencies returned once more. For a number of days very frequent painful urination of clear urine was present and a much more annoying symptom, that is singultus, which, with short intervals, continued during eleven days, greatly sapping the patients strength and unrelieved by any sedative, atropin, alkalies, acids and other drugs. Morphin injection gave relief for a few hours, likewise gastric lavage, this was for several days performed two and three times a day, always removing large quantities of fluid with turbid masses. An attempt to employ duodenal tubing miscarried, the tip remaining in the stomach.

Considering the evidence of disordered calcium metabolism I advised intravenous injections of calcium chloride, 5 cc of a 10 per cent solution, for three days given twice a day, then once a day, then every other day and finally twice a week. Altogether 20 injections were given. After the first injection of calcium chloride the singultus stopped, appetite returned and food intake was tolerated. From now on rapid recovery followed, patient regaining strength, remaining free from all discomfort and adding up to the middle of April, 20 pounds in weight. It is worthy of note that with all the very severe disturbances the lung condition remained stationary and inactive.

**Comment.** The inflammation of the dilated common duct found at operation was of recent date, with fever and jaundice of about thirty hours' duration, while only a week before duodenal drainage had produced a free flow of bile carrying no signs of inflammation. Since no stones were discovered and Vater's papilla proved wide open, it is not stretching imagination too far, to consider the acute cholangitis a result of severe spasm involving the sphincter of the common duct, which also caused acute pancreatitis by a flow of infected bile into the pancreas.

Spasticity is a predominant feature in the history of this patient. From childhood on pronounced tendency to hiccoughs existed and during the period of observation frequent cramps were observed in various parts of the voluntary neuro-muscular apparatus.

Combined with spasmophilia we found evidence of disordered lime metabolism. At one time there was an unusual type of phosphaturia and at another period an increased discharge of lime from the intestines.

*Disordered Calcium Metabolism and Visceral Tetany.* The association of disturbed calcium metabolism and tetany after experimental and operative removal of the parathyroids led to the conception that a change in calcium content causes the increased irritability of the neuromuscular apparatus. There is still a great divergence of opinion regarding the actual relation of parathyroid deficiency and of disordered calcium metabolism, also

regarding the character of the calcium disorder. Some authors assert that in this deficiency the calcium content of the blood is low, while others maintain that the total amount of calcium present in the blood is not as important, as is the quantity of calcium present as free calcium.[13] However that may be, when the parathyroids are involved, we can well imagine, that functional parathyroid insufficiency (of whatever origin) may account for temporary states, both of disordered calcium metabolism and of tetany (analogous to paroxysmal tachycardia). Barker and Sprunt[14] claim that temporary tetany may occur without defective functioning of the parathyroid glands. But let chemical changes making for spasticity once develop in the system, be this an effect or not of parathyroid malfunction, these changes may not only increase the irritability of the voluntary neuromuscular apparatus, but may in a similar way affect the vegetative nerves, a condition for which the term "visceral tetany" has been suggested. In a very interesting study Melchior[15] discusses the very great variability of the picture, which visceral tetany may present according to which part of the vegetative nervous system is particularly involved at a given time.

In our case the spasm occurring shortly before the onset of the acute cholangitis and pancreatitis must have involved Oddi's muscle. Whether during the preceding months the severe abdominal paroxysms were confined to the same locality is very difficult to determine. The varying location and irradiation of the pain point to a changing location of the spasm, for which the picture of renal colic with the onset of phosphaturia gives an illustration. It is possible that the roentgen-ray examination during attacks might have visualized the seat of spasm at a given time. Where this was done it yielded interesting results. Melchior in the paper just quoted reproduces the roentgenogram of a patient suffering from gall stones (later removed by operation), which taken during an attack of pain shows a true gastrospasm, the middle portion of the stomach being tightly contracted into a sausage-shaped form. Three quarters of an hour later the same picture was seen A roentgenogram taken two days later during a pain-free period revealed a normal non-ptotic hook-formed stomach with good tone and with a completely filled out middle portion and antrum. This and similar experiences by Melchior and others should guard us against drawing from roentgenograms taken between attacks, too close conclusions regarding the seat of pain and spasm.

*Visceral Tetany and Pulmonary Tuberculosis.* There is one more interesting feature in the history of this case, the combination

[13] Van Paassen: Nedrl. Tijdschr. v. Geneesk. (Haarlem), 1921, **65**, 1162; Abstract, Endocrinology, 1922, **6**, 132.

[14] Endocrinology, 1922, **6**, 1.

[15] Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1921, **34**, 400.

of visceral tetany with pulmonary tuberculosis. It is a well known fact, that pulmonary tuberculosis is frequently associated with states of gastric irritation and with peptic ulcer. Singer[16] recently reported postmortem findings of peptic ulcer with pulmonary tuberculosis. They showed degeneration and neurotic atrophy of the vagus. Singer considers the anatomical changes of the vagus a product of the tuberculous process. In cases still devoid of manifestations of a lung involvement, he attributes the earlier state of functional vagus derangement to a tuberculous disposition. These cases present only symptoms of gastric irritation and Singer designates the gastric syndrome the sign of latent tuberculosis. One may gain a different aspect of the combination, by considering the possibility, that both, the lung and the gastric disease, are the result of the same underlying general disturbance. The same constitutional makeup, the so-called asthenic habitus, predisposes equally to pulmonary tuberculosis and to derangements of the vegetative nerves. It is possible, that here also disordered calcium metabolism plays a part. We have just discussed its relation to visceral tetany and it may be added that French clinicians lay great stress on demineralization, especially upon the increased discharge of calcium and magnesia as one of the basal factors in the development of pulmonary tuberculosis. One may perhaps find some support for this conception in the favorable reports of the treatment of tuberculous conditions by the systematic intravenous injection of calcium chloride solutions,[17] the same as those which were employed in our case.

*Calcium Therapy.* Finally a few remarks about calcium therapy. I frequently use calcium in the treatment of irritative disorders of the digestive organs, employing large doses of lime water, calcium lactate, the various calcium phosphate preparations, from among which, for a while I used to favor the tribasic calcium phosphate, specially prepared, for it is difficult to procure. During the last few years I have been giving, with preference calcium chloride, a teaspoonful of a 20 per cent solution of crystallized calcium chloride in distilled water, to be taken in half a tumbler of water in the course of the principal meals. I have seen some favorable results, for example in periodical painful gastric hyperacidity, which in certain cases was promptly relieved by the calcium solution. I advise patients subject to periodic hyperacidity and to periods of active ulceration to continue the calcium medication over a course of months, anticipating its prophylactic effect in the same way as it is supposed to act as a preventive of hay-fever.[18] The beneficial effect of a long continued milk diet

[16] Arch. f. Verdauungskr., 1921, **28**, 131.

[17] Maendl: Ztschr. f. Tuberc., Leipzig, 1921, **35**; Abstract, Jour. Am. Med. Assn., 1922, **78**, 137, giving instructions as to technic. See further: Ringer, P. H., and C. L. Minor (Am. Rev. Tuberc., 1922, **5**).

[18] Emmerich, R., and Loew, O.: München. med. Wchnschr., 1915, **62**, 41.

in peptic ulcer and other irritative disorders of the digestive tract is probably in part due to the high calcium content of the milk.

In our case we employed before the second operation both milk diet and the calcium chloride solution, although only for a short period. They failed to make any impression upon the tendency to these severe paroxysms. After the second operation, however, the intravenous calcium administration seemed to stop the very annoying hiccough and the associated retroperistalsis of the upper digestive tract. I have no intention of overstating the importance of a single observation, but this experience should certainly encourage further trials of intravenous calcium therapy in cases of visceral tetany.

Lime therapy is empirical and will remain so until we know more about calcium metabolism and its disturbances. So far our knowledge is scanty. Here is a large field for investigation with the vista, that modern chemistry will establish a solid foundation for the study of calcium metabolism, disorders of which may prove to be the underlying constitutional derangement in the development of local diseases of the digestive tract, as gout is in acute inflammations of joints and diabetes in gangrene.

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## THE CHEMISTRY OF PSEUDOCHYLOUS ASCITES AND OTHER TYPES OF EXUDATES.*

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and

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Milky effusions into the serous cavities are classified into three types: as presented by Rolleston[1] and more recently by Huber[2] and Bradbury.[3] These comprise: (1) *The true chylous*, due to the presence of chyle; (2) *the chyliform* or *fatty*, containing emulsified fat as the result of a fatty degeneration of cellular elements, and (3) *the pseudochylous*, in which the opacity of the fluid is not attributable to a fatty emulsion. Wallis and Schölberg[4] do not consider that groups two and three are distinguishable and preferred to consider them both under the term "pseudochylous."

However, even this differentiation is not accepted by Gandin,[5] who does not believe that the negative chemical tests for fat in the pseudochylous fluids disprove the assumption of the fatty

* Read at the meeting of the American Association for Clinical Investigation, May, 1922.

nature of suspended molecular granules; he considers therefore the terms chyliform and pseudochylous as superfluous.

According to Lee[6] experimental ligation of the thoracic duct in cats leads to the development of collateral lymph paths or new venous anastomoses; accumulation of free fluid in the peritoneal cavity and thorax did not occur. It has for years been assumed that complete or partial obstruction of the duct may induce a true chylous ascites. This experimental work of Lee still further shows our ignorance as to the origin and pathogenesis of even true chylous ascites, though the author admits that "one cannot claim with absolute surety that ligation of the thoracic duct in the human subject would prove equally innocuous."

The opacity of the pseudochylous type of effusion is due to the presence of lecithoprotein, according to Wallis and Schölberg;[4] the lecithin is associated with the globulin fraction. These writers have reviewed 173 cases of milky effusion in the literature, of which 71 were "probably of pseudochylous type." As causes, in order of frequency for this group, they found (1) malignancy, (2) nephritis, (3) cirrhosis of the liver, and (4) tuberculosis.

In reviewing the literature, one is struck by the paucity and insufficiency of the chemical data in even the more recent case reports of milky effusions. Again, emphasis is placed particularly on the differentiation of the types of milky effusions, and little or no attention is given to a comparison of these from a chemical standpoint with the ordinarily encountered transudates or exudates. Bradbury[3] has tabulated from the modern literature up to 1918, the chemical, gross and microscopical characteristics of chyle (9 cases), chylous fluids (10 cases), and pseudochylous fluids (13 cases); the fluids were typed according to the criteria of Wallis and Schölberg with consideration of the clinical descriptions. Recent case reports of milky effusions include contributions by Udaonda and Castex,[7] Udaonda and Carulla,[8] Hendricks,[9] Casaubon,[10] Traub,[11] and Tuohy.[12]

The clinical features and the pathological findings in the case of malignancy with milky ascites, which came under our observation, are quite typical. For comparison, data on 3 cases with ascites where paracentesis was done about the same time are included (Table I). The analysis of the fluid aspirated from the brain tumor case will be discussed later in the paper; these figures are given in the last column of the table. The case histories follow:

Case I.—Watson; aged seventy-six years; widow; clinic No. 9671; admitted December 14, 1921; for five years sudden attacks of nausea and vomiting followed by slight icterus; no colic; radical operation for carcinoma of mamma, August, 1920. Present illness began in November, 1921, with sense of distress and occasional

sharp pain in right upper quadrant; gaseous eructations and constipation; anorexia, loss of weight and strength. On examination some cachexia but no jaundice. Abdomen tense and resistant; free fluid present. No anemia. Gastric subacidity. No occult blood in stools. Gastric series after barium meal negative. Paracentesis, December 17, yielded 3400 cc of milky yellow fluid (Watson I); roentgen-ray therapy. Death January 6, 1922, from progressive cachexia and anuria. Second aspiration one hour post mortem, revealed about 1000 cc reddish-brown fluid (Watson II). Postmortem examination revealed primary carcinoma of gall-bladder with metastases to liver, ovary, pleura, lung and peritoneum with hydroperitoneum.

Case II.—Shoemaker; aged twenty-five years, male; clinic No. 9447; admitted October 8, 1921; rheumatic fever in 1914 with endocarditis followed by gradual onset of cardiac decompensation, until by July, 1921, he was bedridden and remained so until death. Examination revealed an old mitral and aortic insufficiency with general anasarca. On December 2, 1921, paracentesis of 850 cc of cloudy straw-colored fluid and again on December 6, 1921, 3230 cc of similar gross appearance (See Shoemaker). Third paracentesis January 9, 1922, of 330 cc. Death January 10, 1922. Autopsy revealed a healed mitral and aortic endocarditis, an obliterative pericarditis and marked hypertrophy and dilatation of heart.

Case III.—Ball; aged fourteen years, female; clinic No. 9710; admitted December 28, 1921. Scarlet fever in 1915, and chorea in 1917. Tonsillitis in November, 1921; liability to winter bronchitis since pneumonia in infancy. No arthritis. Present illness began November 27, 1921, with edema of legs; on December 11, pain in right upper quadrant where a hard mass could be felt, called a tumor of the liver by the home physician. Examination revealed general anasarca, an enlarged heart, embryocardia and a short systolic bruit at apex; pulmonary edema; an enlarged liver and marked ascites; no jaundice; no anemia; normal urine. Paracentesis on December 30, of 1325 cc of light straw-colored fluid (See Ball). Patient removed December 28, 1921, against advice, with a tentative diagnosis of chronic adhesive pericarditis and cardiac decompensation (Pick's disease).

Case IV.—Mohs; aged twenty-six years, painter; clinic No. 8907. Admitted April 29, 1921. Scarlet fever at sixteen, followed by arthritis of ankles; second attack of rheumatic fever at nineteen. Since then dyspnea, palpitation and edema upon exertion. All symptoms greatly increased since the spring of 1920 and have rendered him a chronic invalid. Examination revealed marked

cyanosis, general anasarca, auricular fibrillation, a much dilated heart without murmurs, an enlarged liver, ascites, albuminuria, etc. On August 18, he developed signs of a mediastinitis, which gradually subsided; for mechanical relief an abdominal paracentesis was done January 9, 1922, and 3000 cc of dark turbid fluid obtained, (see Mohs). Death January 17. Autopsy revealed an enormously dilated heart with an obliterative pericarditis, and a very extensive myocarditis.

Description of the Ascitic Fluids. *Watson I.* The fluid was milky with a very slight yellow tinge. It had no odor. On standing, a slight separation of fibrin occurred; this enmeshed the formed elements—a few fresh red cells, lymphocytes and epithelial cells. On standing at room temperature without aseptic precautions, the fluid was somewhat resistant to putrefaction for several days; with increasing bacterial growth, part of the protein separated as a white flocculent layer on the surface, a phenomenon which might be mistaken for a cream layer.

*Watson II.* The fluid was removed at autopsy one hour after death. It was somewhat less opaque than the previous specimen, but otherwise was not different.

*Shoemaker.* This fluid had the appearance of that of an ordinary ascites; it was somewhat greenish and turbid. A slight separation of fibrin occurred.

*Ball.* When received for analysis, the specimen was three days' old, and considerable bacterial growth was evidenced on microscopical examination of the slightly flocculent sediment. It was of a yellow-green color and without odor. As the fluid was not fresh, sugar and non-protein nitrogenous constituents were not estimated.

*Mohs.* The fluid was of the ordinary character and sediment. A slight formation of fibrin obtained.

*Analytical Methods. Proteins:* By heat coagulation and weighing the water, alcohol, and ether washed precipitates; or by Kjeldahl nitrogen determinations on the tungstic acid (Folin) precipitates; globulin figures are by difference.

*Fatty Acids.* Bloor's method.

*Lecithin Phosphate Acids.* Bloor's method.

*Cholesterol.* Autenrieth and Funk.

*Glucose.* Folin and Wu.

*Non-protein Nitrogen.* Micro-Kjeldahl according to Folin and Wu, but titration of the distillate with N/100 alkali.

*Urea Nitrogen.* Urease treatment and aeration with N/100 sulphuric acid, and titration with N/100 sodium hydroxide.

*Creatinine and Creatine.* Folin and Wu.

*Chlorides.* Rappleys's method.

*Calcium.* Halverson and Bergheim, Tisdall and Kramer.

Determinations of the lipins, sugar, and urea were immediately started on receipt of the specimens in the laboratory. Samples of the fluids with chloroform added as a preservative were kept in the refrigerator to be used for the other determinations, which were promptly undertaken.

TABLE I.—CHEMICAL COMPOSITION OF THE ASPIRATED FLUIDS.

(The analytical figures are gm. per hundred cc or mgm. per hundred cc.)

| | Watson I. | Watson II. | Shoemaker. | Ball. | Mohs. | Kinsolver. |
|---|---|---|---|---|---|---|
| Specific gravity, 20° | 1.020 | 1.025 | 1.014 | 1.018 | 1.018 | 1.037 ($H_2O$ = 1) |
| Total solids | 5.340 | 6.362 | 2.950 | 5.000 | 4.683 | 8.502 |
| Ash | 0.595 | 0.683 | 0.625 | 0.641 | 0.641 | 0.760 |
| Total protein | 3.931 | 3.813 | 1.922 | 3.806 | 3.376 | 6.758 |
| Albumin | 2.150 | 2.575 | 0.790 | 2.217 | 1.640 | 4.006 |
| Total "globulins" | 1.781 | 1.238 | 1.132 | 1.589 | 1.736 | 2.750 |
| Total fatty acids | 0.660 | 0.480 | 0.310 | 0.300 | 0.300 | 0.320 |
| Lecithin, $H_3PO_4$* | 82.500 | 53.300 | 16.700 | 22.200 | 23.000 | 50.800 |
| Net fatty acids† | 0.190 | 0.170 | 0.210 | 0.170 | 0.170 | 0.030 |
| Cholesterol | 0.088 | 0.080 | 0.048 | 0.048 | 0.032 | 0.144 |
| Glucose | 0.100 | 0.105 | 0.100 | ... | 0.148 | 0.060 |
| Non-protein nitrogen | 36.500 | 350.000 | 42.000 | ... | 98.000 | 40.000 |
| Urea nitrogen | 10.000 | 180.000 | 14.000 | ... | 33.600 | 15.000 |
| Uric acid | 3.700 | 14.000 | 3.900 | ... | 8.000 | 4.350 |
| Creatinine | 1.200 | 3.800 | 0.830 | ... | 1.080 | 0.830 |
| Creatine‡ | 2.000 | 9.500 | 1.670 | ... | 2.100 | 1.500 |
| Chlorides as NaCl | 0.600 | 0.630 | 0.685 | 0.670 | 0.620 | 0.630 |
| Calcium | 7.300 | 7.600 | 7.000 | 7.500 | 7.000 | 9.000 |

* These figures multipled by 8 gives approximate lecithin contents.
† After substracting lecithin fatty acid.
‡ As creatinine.

The data on the Watson fluids (Table I, columns 1 and 2) when judged by the "determining points" of Wallis and Schölberg, are consistent with the criteria for the pseudochylous type except for the high specific gravity and protein content (Table II). However, the source of the effusion must be considered; pleural, peritoneal, cutaneous and cerebrospinal fluids show relative differences in the protein concentration. Again, differentiation by the protein content or the specific gravity of pseudochylous and chylous fluids should be very questionable. Lymph concentration in protein would depend on the permeability of the endothelial walls of the vessels and would be influenced by toxic injury to these.

The proportion of serum albumin to serum globulin might vary according to quantitative differences in the blood proteins (Umber[13]) though influenced by the relative viscosity which determines the ability of these proteins to pass through the capillary walls (Oswald[14]). Accordingly, it would be expected that effusions in cases where the blood plasma contained little serum albumin (amounts only slightly over 0.1 per cent have been noted) would

have a low total protein content with a very high ratio of the globulin to the albumin. Such fluids are found in the literature. Epstein[15] even reports one peritoneal fluid (nephritic) of very low total protein content (0.285 per cent) in which serum albumin was not present. It may be said that attempts have been made to correlate the proportion of globulin to albumin in ascitic fluids with the clinical conditions which invoked these (Joachim[16]).

TABLE II.—CRITERIA OF WALLIS AND SCHÖLBERG APPLIED TO OUR CASE (WATSON).

(The *plus* signs mark the characters that obtain for our milky ascitic fluids Watson I and II.)

| | Chyle.* | Chylous fluids. | Pseudochylous fluids. |
|---|---|---|---|
| Specific gravity | 1.022 | + Over 1.012 | Under 1.012. |
| Total solids | 6.785 | + 4 per cent or more | 2 per cent or less. |
| Total protein | 3.640 | + 3 per cent or more | 1 to 3 per cent. |
| Serum albumin | ... | + Mostly. | |
| Serum globulin | ... | Traces only | + Appreciable amounts |
| Fats | 2.990 | 0.4 to 4 per cent | + Low. |
| Lecithin | 0.310 | Traces only | + Characteristic. |
| Cholesterol | 0.490 | Always present | + Occasional. |
| Sugar | ... | 0.36 to 0.00* | 0.196 to 0.00.* |
| Salts | 0.740 | As in chyle | As in lymph. |
| Color | ... | Yellowish | + White. |
| Opacity | ... | Same each tap | + Varies each tap. |
| Odor | ... | Slight, like food | + None. |
| Microscopic cells | ... | Very few | + Vary, may contain fat. |
| Microscopic fat | ... | Fine fat globules | + Granules, not fat. |
| Cream layer | ... | Usual | + Not usual. |
| Freezing point | ... | About −0.51 | −0.56 to −0.61. |
| Sediment | ... | None | + Usual. |

* Bradbury's compilation.

The most striking of the chemical "determining points" seem to be (1) the high content in lecithin, which is associated with the so-called globulin fraction,* (2) the low fatty acid figure and the uniformity of the fatty acid content after allowing for the lecithin fatty acid, and (3) the low cholesterol figures. True chylous fluids would seem to contain cholesterol in quite appreciable amounts, probably because of absorption of food and bile cholesterol from the intestine into the lacteals. Mueller[17] found that there resulted an increase in both cholesterol and cholesterol esters in the chyle of dogs when either one was added to the diet.

It may be noted that the milky ascites differs from our other peritoneal fluids particularly in the higher content of lecithin-phosphoric acid and of cholesterol; however, the cholesterol con-

* The filtrates containing the serum albumin after precipitation of the fluid (five-fold diluted) with an equal volume of saturated ammonium sulphate solution were water clear.

tent of the Watson fluids is lower than that of blood plasma or even than that in the acute exacerbation of pernicious anemia. Inasmuch as Horiuchi[18] has shown that experimentally induced lipemia in rabbits may increase the plasma lecithin up to seven and the cholesterol up to eight times the normal values, an explanation for the formation of transudates that are pseudochylous is suggested when such conditions obtain.

Calcium in excess in protein combination is apparently not responsible for any of the opacity of the pseudochylous fluid, being present in all of the specimens in but little less concentration than in normal blood plasma. Wallis and Schölberg's figures (recalculated as calcium) are 18 and 12 mgm. per cent respectively for their white fluids in order of opacity, and but 2 and 3 mgm. per cent for the less milky specimens; they do not discuss their calcium results in this connection.

Of particular interest are the very high non-protein nitrogenous constituents in the second Watson fluid, due to anuria; a moderate degree of non-protein nitrogen retention obtains for Mohs also.

Kast and Killian[19] found that many advanced cases of malignancy, possibly as the result of the toxemia, give the chemical blood picture of moderately severe nephritis with a hyperglycemia and lowered carbohydrate tolerance; the termination of some of their cases was typically uremic.

Denis and Minot[20] have shown that the non-protein nitrogenous substances in transudates and exudates vary with the concentrations in the blood; they did not work with nitrogen retention cases. Recently Weiss and Garner[21] reported a case of nephritis with unusually high progressive nitrogen retention; their data include urea nitrogen determinations, which approximate the blood findings,* on the cerebrospinal and pericardial fluids. Our total non-protein nitrogen estimation on the Watson II, specimen and on Mohs also is relatively very high as compared with the urea nitrogen figure; the residual nitrogen probably represents amino-acids, and a separation of characteristic crystals of leucin and tyrosin actually occurred in the second pseudochylous fluid.

A specimen of a fluid aspirated from the brain was subjected to the same analytical procedures as were the ascitic fluids. A brief summary of the clinical findings for the case (Kinsolver) follows:

CASE V.—Kinsolver; aged twenty-five years, farmer; clinic No. 9730; admitted January 4, 1922; first noted headache, nausea and vomiting November 1, 1921, which gradually recurred at more frequent intervals. In February, 1921, syncopal attack without convulsion. Subsequently three or four attacks of loss of consciousness and generalized convulsions beginning in the legs;

* The total non-protein nitrogen twelve hours before death was 401 mgm., of which urea nitrogen represented 75.8 per cent.

some failure of vision and mental irritability. Examination by Dr. van Epps revealed a marked Romberg sign and reeling gait; coarse tremor of hands. Marked bilateral choked disk, more advanced in right. Blood and spinal fluid negative in all respects. On January 13, 1922, under local anesthesia a small trephine opening near midline in frontal region was made. A needle was passed through the intact dura for one and one-eighth inches and entered an area containing fluid under pressure. This was removed by the two-way syringe and equal amounts of air were introduced without discomfort. The stereoscopic plates revealed a large cyst in the frontal region taking origin at the base of the brain in the region of the pituitary. This had been tapped instead of the ventricles. As the site of the cyst rendered the removal extremely hazardous, the patient was discharged temporarily relieved of his pressure symptoms.

The specimen was received in the laboratory promptly after aspiration and was in volume 45 cc. It was a slightly orange-yellow fluid, very clear, and without sediment except for glistening suspended cholesterol crystals. It did not clot, even on standing for the period of the analytical examination. An occult blood test (Meyer's) was negative.

The analytical data (Table I, the last column) show a fluid similar to blood serum of rather high specific gravity and total solid content, of which the protein approximates 80 per cent. In spite of the cholesterol crystals in suspension, the cholesterol content is not above that of blood plasma. Allowing for the fatty acid combined as lecithin (as dioleal lecithin), the neutral fat content must be practically *nil*. The amount of sugar present is about that of normal cerebrospinal fluid. The uric acid is a little high as compared with normal blood. The presence of cerebrins could not be demonstrated.

The xanthochromia and the high protein content of the specimen recall the fluid compression of the types described for the spinal cord as the syndromes of Froin and of Nonne (Sprunt and Walker[22]). The fact that the cerebrospinal fluid was essentially normal indicates an intraventricular cul-de-sac or a cyst. Wells[23] states that the presence of cholesterol crystals in aspirated fluids may be attributed either to relatively old processes involving cellular degeneration, or to the resolution of a large blood extravasation. It is probable that we are dealing with a degenerating brain tumor replaced by a gradually concentrating transudate. The fibrinogen has either not passed into the fluid or has been deposited as fibrin on the wall of the cavity. The xanthochromia should be due to the ordinary plasma pigments. However, the similarity of the glucose content to that of cerebrospinal fluid is perhaps not without significance.

Finally, we would recommend the more frequent complete chemical investigation of all transudates or exudates because of the valuable diagnostic and indeed prognostic assistance sometimes obtained.

**Summary and Conclusions.** The chemical composition of a milky peritoneal fluid from a case of malignancy, and the comparative data of three cases with serous ascites are presented.

The milky effusion is characterized by its high content of lecithinphosphoric acid and to a lesser degree of cholesterol. Net fatty acid figures are low for all the fluids.

Calcium in protein combination is not responsible for the opacity of the fluid.

Milky fluid obtained at necropsy one hour after death following three days of anuria has a non-protein nitrogen partition such as is found for the blood in severe retention cases.

It is concluded that the milky fluid obtained in our case is a true pseudochylous ascites.

A specimen of a yellow fluid aspirated from an intra-ventricular cyst or ventricular cul-de-sac of the brain was subjected to the same analytical procedures as were the ascitic fluids. The figures are included in this report.

*Addendum.* Since the report was sent to this journal, we have studied the aspirated contents of a cyst of two months standing in the groin of a man, aged twenty-five years, (Case F. A., No. 51486). About 150 cc of a viscous, slightly turbid, light straw-colored fluid were obtained. Smears, cultures and guinea-pig inoculation were negative. The fluid is of particular interest because of its content in mucin, when an epithelial origin can hardly be presumed in this instance. The mucin was identified by precipitation with acetic acid and yielding on acid hydrolysis abundant reducing substances without sulphate formation. The glucose content of the fluid was notably low. Analytical figures follow:

COMPOSITION OF MUCIN-CONTAINING FLUID ASPIRATED FROM THE GROIN.

| | | | |
|---|---|---|---|
| Specific gravity | 1.030 | Cholesterol | 0.22 |
| Total solids | 7.890 | Glucose | 0.02 |
| Ash | 0.570 | Non-protein nitrogen | 30.80 |
| Total protein | 5.890 | Urea nitrogen | 14.70 |
| Albumin | 3.250 | Uric acid | 5.40 |
| Globulins | 1.080 | Creatinine | 1.50 |
| Mucin | 1.570 | Creatine | 1.20 |
| Fatty acids | 0.177 | Chlorides as NaCl | 0.58 |
| Lecithin, $H_2PO_4$ | 30.800 | Calcium | 6.70 |

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# THE CARDIOVASCULAR COMPLICATIONS OF KYPHOSCOLIOSIS WITH REPORT OF A CASE OF PAROXYSMAL AURICULAR FIBRILLATION IN A PATIENT WITH SEVERE SCOLIOSIS.

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The functional disturbances of the circulation and of respiration, which are associated with kyphoscoliosis, do not receive the attention which they merit, in spite of the fact that they have been studied by many authors. I wish to review briefly the important literature on the subject and to present a rather unique case which affords a number of interesting problems.

Hippocrates[1] recognized that dyspnea is a common finding in these patients. In his chapter on the articulations he says, "and in those cases where the gibbosity is above the diaphragm, they become affected with difficulty in breathing. And yet many of them have borne the affection well and have enjoyed good health until old age, more especially those persons whose body is inclined to be plump and fat; a few of them have lived to beyond sixty years of age, but the most of them are more short-lived."

Pathology. Two famous clinicians of the 18th century, de Sauvages[2] and Cullen,[3] mention gibbosity as one of the causes of dyspnea. Bouvier,[4] however, was apparently the first to seek a rational explanation of this phenomenon. In a publication in 1858, he notes that patients with kyphoscoliosis are subject not only to dyspnea but to attacks of asthma, stubborn coughs, palpitation, cardiac arrhythmia and a tendency to syncope, and makes the significant observation that death is usually due to cardiac failure. Sixteen years later[5] in another review of the subject, he states that dilatation of the right chambers of the heart is a very frequent pathological finding in scoliosis. Many years previously Corvisart[6] observed dilatation of the right auricle and ventricle in an autopsy of a hunchback, who had died with symptoms of cardiac dilatation. He attributed it to the increased resistance offered by the distorted bloodvessels in the chest.

Traube[7] was the next to find on autopsy hypertrophy and dilatation of the right ventricle in a patient with a greatly deformed chest, who, before his death, had severe dyspnea and cyanosis, swelling of the jugular veins and oliguria. Since that time further evidence of the frequency of organic heart lesions, as well as of symptoms referable to the heart, has accumulated. Thus Rieder[8] found hypertrophy and dilatation of the right ventricle in 29 of 35 cases autopsied on Virchow's service. Eleven cases showed a hypertrophy and dilatation of the whole heart and 5 a small atrophic heart. Four patients exhibited fatty degeneration of the heart.

Similar findings were reported by May,[9] Poissonier,[10] Barié,[11] Fräntzel[12] and more recently by Meyer.[13] The most complete investigation, however, is to be found in the exhaustive monograph of Bachman,[14] published in 1899. Bachman made an intensive study of 197 of his own cases which came to autopsy, as well as of 79, which he found recorded in the literature. Of the total of 276 cases, 247 or 89.5 per cent presented an organic lesion of the heart or pericardium, but only 13 had organic valvular defects. In 154 cases the heart was examined more carefully to determine the nature of the hypertrophy and dilatation. Of these 154 cases, 87 or 56.4 per cent had hypertrophy and dilatation of the right ventricle, 27 or 17.5 per cent of the left ventricle, and 40 or 25.9 per cent of both ventricles. Bachman also noted that displacement of the heart upward and in the opposite direction to the

scoliosis is very frequent. This cardiac displacement results not infrequently in a marked tortuous and angular deviation of the aorta, the large vessels and the inferior vena cava. The aorta usually follows the curves of the spine. Kinking of a subclavian artery may cause inequality of the pulses. The right auricle shares the dilatation of the right ventricle and at times harbors thrombi, which may result in pulmonary embolism. Of 195 deaths which Bachman studied, 116 or 59.4 per cent were due to cardiac failure; 24 were due to tuberculosis.

Romberg,[15] in a study of 38 patients with kyphoscoliosis, found death due to myocardial insufficiency 26 times. Ljungdahl,[16] in addition to the hypertrophy and dilatation of the right ventricle, observed a dilatation and moderate arteriosclerosis of the pulmonary artery in 2 cases which came to autopsy.

The mechanism by means of which these pathological lesions are brought about is easy to understand. The deformed thorax is smaller than normal in size, the diaphragm is usually high. Moreover, because of the fact that the thoracic distortion is well established before bodily growth is completed, the chest lags behind the rest of the body in development. As a result of these factors the lung volume is greatly encroached upon, with ensuing atelectasis of large pulmonary fields. The capillary bed is further lessened by the constant presence of emphysema in the non-atelectatic portions of the lung. Not infrequently a chronic bronchitis is superadded and serves to obstruct the flow of the blood to a still greater degree. As a result of the diminution of the pulmonary stream bed, the pressure in the pulmonary artery becomes elevated. This is followed in time by dilatation of the pulmonary artery, often accompanied by more or less arteriosclerosis, and by dilatation and hypertrophy of the right ventricle and right auricle.

There is still another factor which places more work upon the heart. In the normal person the negative pressure in the thorax, established by each inspiration, facilitates the flow of venous blood into the right auricle and of blood from the pulmonary capillaries into the left auricle. The elastic recoil of the lungs on expiration is a further aid in the movement of the blood from the right to the left side of the heart. In patients with kyphoscoliosis the respiratory excursions of the thorax are greatly limited and so this accessory aid to the circulation is rendered negligible.

Some authors believe that owing to the factors just mentioned, an insufficient amount of blood reaches the left ventricle and explain in this manner the occasional finding of a small left ventricle in these patients.

These obstructions of the lesser circulation eventually result in insufficiency of the right ventricle, just as a long continued peripheral hypertension brings about failure of the left ventricle. Failure of the right side of the heart is seen not infrequently in a number

of diseases which obstruct the flow of blood in the lesser circulation. Among the most common of these are pulmonary emphysema, particularly when associated with chronic bronchitis, fibroid phthisis and extensive pleural adhesions.

Symptomatology. The usual symptoms are dyspnea, cyanosis and edema of the legs. Dyspnea commonly makes its appearance within a few years of the establishment of a well marked deformity. It is due in part to the pulmonary atelectasis and emphysema, but when it grows more pronounced myocardial insufficiency becomes the most important factor. The vital capacity of the lungs is usually greatly diminished. The patients often complain of palpitation, precordial pain and vertigo. The attacks of palpitation and pain may come in crises. The pulse not infrequently is rapid and may be irregular. Sottas[17] published a number of clinical histories of patients in whom the pulse rate varied from 112 to 120. In many cases reported by him and others the rhythm was very irregular but no careful description of the irregularity can be found in the literature, except in the case of one of Sotta's patients, who had many extrasystoles. One gains the impression, however, from some of the case reports that the arrhythmia was due to auricular fibrillation. As the myocardial insufficiency progresses, dyspnea, cyanosis and edema become more marked, the liver becomes enlarged, oliguria is noted, and anasarca and ascites may set in.

The physical signs are for the most part inconclusive because of the great deformity of the chest. It is almost impossible to ascertain the presence or absence of cardiac hypertrophy, and murmurs are difficult to interpret. The pulmonic second sound is usually definitely accentuated. The lungs in advanced cases show signs of congestion.

Prognosis. The prognosis in patients with kyphoscoliosis depends in a large measure upon the reserve power of the heart. Of course, not every patient develops a cardiac lesion. They may live for years complaining of nothing but dyspnea on exertion. Once the signs of myocardial insufficiency are well established, the prognosis becomes poor. Intercurrent pulmonary infections, by adding an extra load on the laboring heart, frequently precipitate the end. Women, apparently, survive their disability longer than men. In Bachman's series of 111 men, the average age at death was forty and one-tenth years, and of 158 women, the average age at death was fifty-two years. Romberg, in a much smaller series of 15 men, found the average age at death thirty-nine and seven-tenth years, and of 11 women fifty-four and six-tenth years.

**Case Report.**—The following case was observed at the Montefiore Hospital:

The patient is an unmarried woman aged twenty-nine years, weighing 72 pounds. When she was aged nine years, her mother noticed that the right shoulder was higher than the left. The

deformity of the spine was first noted when she was aged nine years and six months. This has become slowly but progressively worse, in spite of the application of all kinds of casts and braces. No pain or other symptoms referable to the spine. For ten years the patient has had attacks of dizziness, appearing every six months. During the past year the dizziness has become worse and very frequent. The vertigo lasts about twenty-four hours and the patient has to be confined to bed. "Everything before me is blurred and the room is in a constant whirl." During the same period she has had headaches three or four times a week accompanied by nausea and vomiting. For about five years dyspnea on exertion has been apparent.

Physical examination on September 30, 1920: There is a marked scoliosis with a right dorsal and a left lumbar curve. The chest is very prominent on the right side posteriorly and is drawn in, in the left axilla to form a deep groove. There is a systolic murmur over the aortic area. The pulse is regular and of good quality, rate 110. Urine shows a faint trace of albumin and occasional hyaline casts. The Wassermann reaction in both blood and spinal fluid is negative. Blood pressure 134/80.

June 10, 1922. During her stay in the hospital this past year and a half, the patient has shown little improvement. Her weight has remained stationary and the attacks of vertigo and headache still incapacitate her at frequent intervals. On May 13, 1922, she was placed on a strict Weir Mitchell rest cure. Her progress during the first two weeks was very satisfactory. She assimilated large quantities of food and gained 5 pounds in weight. Quite suddenly, on May 31, she complained of severe palpitation and shortness of breath. A few hours later she had her supper but vomited immediately afterward and the palpitation and dyspnea became greatly aggravated. She was in great distress and felt as though death were imminent. On physical examination she appeared pale and bathed in a profuse perspiration, respirations were rapid, rate 30. The heart action was absolutely irregular, the apex rate was 160, the radial rate 120. The following day the subjective symptoms were less severe but auricular fibrillation persisted and was proven electrocardiographically. On June 2, the heart action was again regular but rapid. For a week following the attack the patient has been very nervous and has complained a good deal of palpitation. She fears the onset of another attack, which, she believes, will be fatal. The pulse rate is uniformly rapid, between 120 and 150, but can be slowed to 70 by pressure on the right eyeball. The palpitation becomes aggravated from time to time, the patient stating that her heart begins to "bang." For the first four days after the attack the patient was often cyanotic, which cyanosis at times would alternate with pallor. There has been no edema of the legs. On June 5, she had an attack of

intense vertigo, which persisted for three days and was accompanied by occasional vomiting. During the attack of vertigo, objects appeared to move from right to left. She complained of a sense of oppression in the epigastrium.

Physical examination on June 7, revealed the patient lying on her left side. She always assumes this posture when complaining of dizziness. The face is rather flushed but not cyanotic. The lungs show emphysema, except in the right chest posteriorly, where breathing is somewhat diminished. No rales are heard. The apex impulse is in the fifth interspace, 9 cm. from the midsternal line. The left border is 10.5 cm. from the midline at the sixth rib and 7 cm. out in the third interspace. The right border is 4 cm. from the midsternal line. A systolic murmur is heard at the aortic area and at the apex. Both are widely transmitted. The pulmonic second sound is markedly accentuated. The upper border of the liver is at the fourth rib in the midclavicular line, the edge, which is tender, is 8 cm. below the xiphoid in the midline, total length 15 cm.

The pulses are equal, regular and rapid. There is some tortuosity and thickening of the right temporal artery. The following table shows the average pulse rates for several months during her stay in the hospital.

October, 1920, 105.
March, 1921, 119.
October, 1921, 116.
March, 1922, 110.

On May 29, 1922, the pulse rate become more rapid, varying between 124 and 140, until the onset of the fibrillation. Since the restoration of normal rhythm the average pulse rate has been 141. Respirations have averaged 29. An electrocardiogram taken March 22, 1921, showed a tendency toward right ventricular preponderance with P in Lead II, increased in amplitude. Electrocardiogram on June 1, 1922, showed auricular fibrillation with a tendency to right ventricular preponderance. Electrocardiogram taken on June 16, 1922, showed definite right ventricular preponderance. The blood nitrogen, the basal metabolic rate, and the eyegrounds are normal. There has been no fever at any time during one and one-half years' stay in the hospital. A roentgen-ray of the chest gives no conclusive idea of the size of the heart because of the great distortion of the spine and ribs.

June 15, 1922. For three days the patient has felt quite comfortable. Pulse regular, rate about 110. It is difficult to determine with accuracy the cause of the circulatory disturbances in this patient. Physical examination and roentgen-ray findings are inconclusive because of the deformity of the chest. It is impossible to estimate the significance of the murmurs. The rapid pulse is apparently not dependent upon myocardial disease because it can be controlled so rapidly by vagus pressure. The

electrocardiographic finding of a right ventricular preponderance suggests that in this case, just as in most other cases reported in the literature, the right ventricle is laboring under an increased resistance. It is probable that the right auricle became greatly dilated, which paved the way for the attack of paroxysmal auricular fibrillation. The longstanding headaches and vertigo, which have been observed by other authors as well, may possibly be explained by circulatory disorders of the brain.

Among the lesions found by Bachman in his large series of autopsies are cerebral hyperemia, edema or anemia, internal hydrocephalus, pachymeningitis or leptomeningitis. He believes that any one of these pathological conditions may account for the attacks of headaches and dizziness.

**Summary.** Attention is called to the frequent visceral disturbances which accompany severe kyphoscoliosis. Hypertrophy and dilatation of the right chambers of the heart, followed by signs and symptoms of myocardial insufficiency are common sequelæ. A case is described with paroxysmal auricular fibrillation and symptoms of myocardial insufficiency.

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# ABSORPTION FROM THE URINARY BLADDER.

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In a series of experiments performed for the purpose of discovering whether bacteria would pass through the various component portions of the urinary tract, it was necessary to perform control experiments in order to determine whether the experimental procedures had damaged the structure under observation. Phenolsulphonephthalein was employed with the bacteria, and its elimination from the kidney observed. The results of the experiments with regard to the passage of bacteria from the urinary tract have been reported elsewhere.[46, 47]

The review of the work of previous investigators on absorption from the urinary tract demonstrated (1) The extensive investigations on the subject; (2) the marked contradictory results; and (3) the paucity of references to the subject in American literature. This applied particularly to absorption from the urinary bladder, and since our results were so definite on this phase of the problem, we feel justified in presenting them.

**Previous Investigations on Absorption from the Urinary Bladder.** We found it impossible to review all of the voluminous literature on the subject, but believe that the more important researches are included in our bibliography.[1–70]

The ancients were said to have considered the bladder as being capable of absorption, but a definite conception of such a function seems not to have developed until about the middle of the eighteenth century. Experimental observations on the subject were made as early as 1779. The first conception of the subject was a physiological one, and the bladder was believed to absorb some of the constituents of the urine and thus produce a concentration of this excretion. Difference in quantity, color, amount of solids and other qualities in urine secreted by night and by day were explained on the basis of more absorption of fluid during the night. At the beginning of the nineteenth century, a practical aspect of the question developed in the possibility of administering drugs by the bladder.

While most investigators were able to obtain evidence that absorption occurs through the bladder mucosa, others were not able to obtain positive results. Thus, two groups of investigators were formed; one claimed that there is absorption through the

bladder, and the other that the bladder mucosa is impermeable. The group obtaining negative results attempted to explain the positive results on the basis that the operative procedure, or the insertion of the catheter, traumatized the bladder mucosa, and that the trauma allowed the test substance to pass out of the bladder. This idea led to the study of absorption from a previously traumatized bladder. Practically all investigators of absorption from bladders with traumatized mucosa obtained positive results. Thus a third group was formed who claimed that normal bladders will not absorb, but bladders subjected to trauma will absorb. Each of these groups has its representative in recent literature.

Many operative procedures have been devised for preparing the bladder to test its power of absorption. The first experiments were evidently rather crude. In many instances, little or no precaution was taken to prevent the substance from coming into contact with the mucosa of other portions of the urinary tract. It also was possible that in some experiments the operative procedure damaged the blood supply to the bladder. However, in most of the experiments, such possibilities for error seem to have been eliminated. In many instances the experiments were carried out on human beings. Other investigators used animals, including guinea-pigs, rabbits, cats and dogs.

Many substances have been employed in the tests. They include distilled water, normal salt solution, dextrose, saccharose, sodium chlorid, sodium iodid, sodium ferrocyanid, sodium salicylate, mercuric chlorid, ferric chlorid, lithium chlorid, potassium iodid, potassium cyanid, potassium ferrocyanid, acetic acid, boric acid, carbolic acid, salicylic acid, hydrogamic acid, carbon monoxide, carbon dioxide, hydrogen sulphite, ether, chloroform, alcohol, chloral hydrate, strychnine, atropine, cocaine, morphine, curare, pilocarpine, eserine, veratrine, nicotine, cantharides, antipyrine, urea, uric acid, albumen, milk, bacteria, diphtheria toxin and antitoxin, and methylene blue. It is readily seen that most of these substances were employed because they exerted a definite physiological action. Certain of them were selected because they could readily be detected in the blood stream; others were chosen for various reasons; a number seem to be of very little value.

The majority of investigators obtained more or less definite evidence that the mucosa of the bladder absorbed. In many experiments it was evident that very little substance was absorbed; approximately 20 per cent of the investigators were unable to obtain evidence of absorption. A careful analysis of all the data presented failed to reveal why contradictory results were obtained. The following points, however, are pertinent with regard to this. The rapid and marked response to the test substance in some instances might have been because the substance was allowed to come in contact with the mucosa of portions of the urinary tract

other than the bladder. Some of the negative results might be due to (1) Injury to the blood supply of the bladder; (2) employment of test substances which could be detected only with difficulty, or which must be in a high concentration in order to cause definite reaction; and (3) the selective absorption by the mucosa of the bladder.

Injury to the blood supply of the bladder would prevent the normal action of the mucosa, and also prevent the entrance of the substance to be detected into the blood stream. If the bladder absorbed the substance slowly its concentration in the blood stream would be low. If the substance could be detected by its physiological activity, or otherwise in small amounts, a positive result might be obtained. If, however, large amounts of the test substance were required for detection, the amounts absorbed would be too small to give positive results. It is known that various portions of the gastrointestinal tract absorb different substances. There is no valid reason why the mucosa of the bladder might not also have a similar capacity.

Various methods have been used to traumatize the mucosa of the bladder, or to produce acute cystitis for the purpose of studying absorption. Usually cantharides, turpentine, acetic acid, or sulphuric acid, were used to produce acute inflammation of the bladder. The substances were injected into the bladder at various times before the final experiments of testing the absorption. In some investigations the urethra was blocked to produce back pressure on the bladder and thus damage it. In some instances it was claimed that the insertion of a catheter into the bladder caused enough trauma to allow absorption.

It often happens that the amount of work done on a problem represents, in inverse proportion, the actual knowledge of that subject. When the results of a series of experiments, devised to give the answer to a problem, are definite, the first published report of such results is often the last because all succeeding investigations are corroborative in character. When, however, the results are not definite and slight changes in the condition of the experiment bring about either positive or negative results, opposing groups of investigators are formed who vie with each other in devising methods and performing experiments to prove their particular answer to the problem. The problem of absorption from the urinary bladder with its accumulation of research experiments and contradictory data is a good illustration of this point. After allowing for errors in technic and methods of investigation, there is no doubt that some investigators obtained evidence of absorption from the bladder, but slight changes in method, test substances, or the physiological condition of the animal could readily have made the result of the experiment negative. This, in itself, would almost imply that the answer to the problem is not of much significance.

**Method of Experimentation.** All experiments were made on dogs maintained under constant ether anesthesia throughout the experiment. Water was administered by stomach tube three to four hours before beginning the experiment in order to insure a flow of urine. The bladder and ureters were exposed through a low median incision. Constancy with regard to the amount of

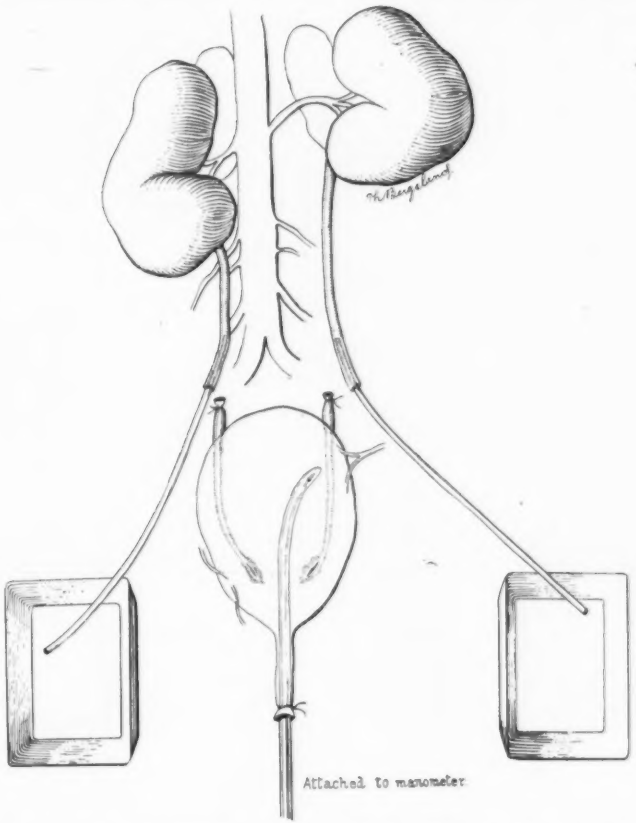


FIG. 1.—Method of introducing dyes into the urinary bladder under constant pressure.

dye in the bladder was secured by one of two methods. In one series of experiments the solution in the bladder was kept under constant pressure (Fig. 1). Both ureters were ligated and sectioned at their point of entrance into the bladder. A hard catheter was inserted into the urethra (all dogs in this series were females), and held firmly in position by a ligature placed on the bladder side

of the urethral opening. A glass T-tube was attached to the catheter. One arm of the tube was attached to a burette and the other arm to a straight glass tube about 25 cm. in length, with an internal bore of approximately 2.5 mm. and graduated markings in millimeters (Fig. 2). The dye was injected into the burette until the pressure in the bladder, as shown by the graduated tube, reached a definite point (7 to 15 cm.). In the second series of

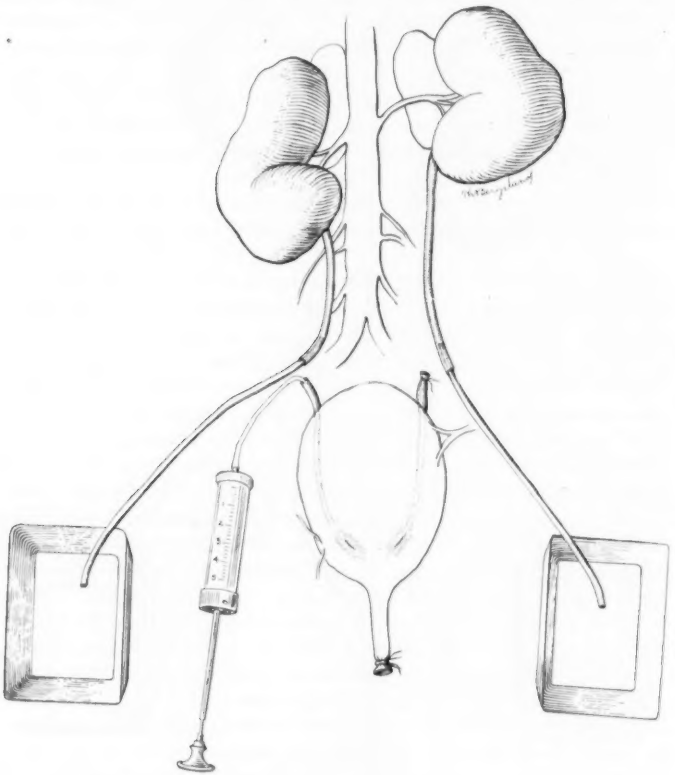

FIG. 2.—Manometer.

experiments the urethra was ligated so that the dye could not reach the urethral mucosa (Fig. 3). One ureter was ligated and sectioned at its point of entrance into the bladder; the other was ligated about 2 cm. from its point of entrance into the bladder, and the dye was injected with a syringe into the bladder by passing a hypodermic needle into the lumen of the ureter on the vesical side of the ligature. After injection the ureter was also ligated

and sectioned at its point of entrance into the bladder. An amount of dye equal to about 20 per cent of the capacity of the bladder was injected. In both series of experiments urine was collected from both ureters by a ureteral catheter. The time the dye was

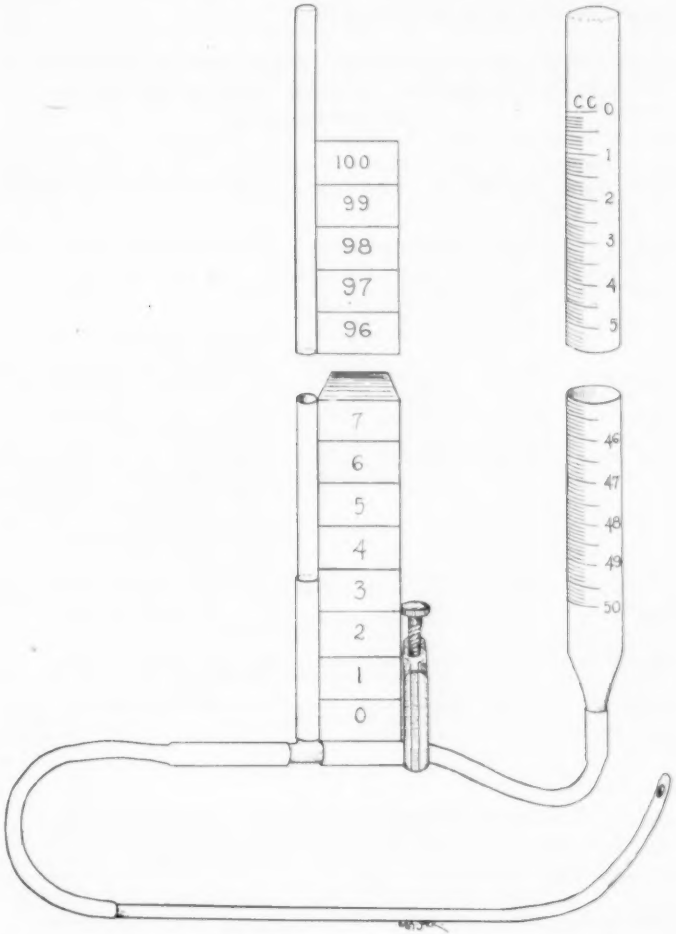


FIG. 3.—Method of introducing a given amount of dye into the urinary bladder

introduced into the bladder was accurately recorded and the urine was tested repeatedly for the dye. In some experiments indigocarmine or methylene blue was used with, or in place of, phenolsulphonephthalein.

By this technic the possibility of technical errors was avoided. The dye could only come into contact with the bladder mucosa, which was not traumatized. The bladder was only partially filled and never distended. If the dye escaped outside the bladder, it could only do so by passing through the mucosa under conditions which were physiologically possible.

TABLE I.—RESULTS OF SERIES OF EXPERIMENTS IN WHICH DYE WAS INTRODUCED INTO THE BLADDER UNDER MEASURED AND CONSTANT PRESSURE.

| Experiment. | Pressure in bladder of water, cm. | Condition of bladder. | Dye used. | Appearance of dye. | Apparent amount of dye. |
|---|---|---|---|---|---|
| 234 | 7 | Acute cystitis | Phenolsulphonephthalein, 5 cc; besides 25 cc culture B. prodigiosus | 26 min. after injection | Small. |
| 236 | 7 | Acute cystitis | Phenolsulphonephthalein, 5 cc; besides culture B. prodigiosus | None | None. |
| 268 | 8 | Normal | Phenolsulphonephthalein, 5 cc; besides culture B. prodigiosus | Trace from right ureter in 8 min.; from both ureters in 15 min. | Medium. |
| 275 | 7 | Normal | Phenolsulphonephthalein, 5 cc; besides culture B. prodigiosus | From right ureter in 50 min.; from left in 65 min. | Trace. |
| 276 | 7 | Normal | Phenolsulphonephthalein, 5 cc; besides culture B. prodigiosus | From left ureter in 55 min.; none from right | Small. |
| 339 | 7 | Normal | Phenolsulphonephthalein, indigocarmine (10 cc) | Indigocarmine from both ureters in 15 min.; trace after 1 hr. and 30 min.; sodium hydroxide added and phenolsulphonephthalein is present in urine from both ureters | Phenolsulphonephthalein large; indigocarmine large. |
| 351 | 10 | Normal | Indigocarmine, 10 cc; besides culture B. prodigiosus | From both ureters in 23 min. | Large. |
| 361 | 7 | Normal | Phenolsulphonephthalein diluted 1 to 6 with water, 5 cc | From both ureters in 16 min. | Small. |
| 363 | 7 | Normal | Phenolsulphonephthalein diluted 1 to 6 with water | From both ureters in 16 min. | Trace. |
| 403 | 12 | Normal | Phenolsulphonephthalein diluted 1 to 6 with water (13 cc) | From both ureters in 15 min. | Small amount; quantitative estimation about 1 per cent phenolsulphonephthalein excreted from both ureters in 2 hrs. |
| 412 | 12 | Normal | Phenolsulphonephthalein diluted 1 to 6 with water (18 cc) | From right ureter in 25 min.; none from left; left kidney found absent at necropsy | Quantitative estimation about 2 per cent phenolsulphonephthalein excreted from right ureter in 2 hrs. |
| 421 | 12 | Normal | Indigocarmine, 5 cc | From both ureters in 30 min. | Small. |
| 672–20 | 15 | Normal | Methylene blue diluted 1 to 4 with water (10 cc) | From both ureters after 2 hrs. | Trace. |
| 673* | 12 | Normal | Methylene blue diluted 1 to 2 with water (27 cc) | From both ureters in 28 min. | Large. |

* Bladder filled with high pressure, then pressure lowered.

**Results of Experiments.** Nineteen experiments were performed. In three experiments we were unable to obtain evidence that the

dye had passed outside the bladder; in the other sixteen experiments the dye was detected in the urine. The time varied between the injection of dye into the bladder and its appearance in the urine. The earliest appearance of the dye was in eight minutes; in some experiments it was not detected for more than an hour; but in most instances it appeared in the urine in from fifteen to thirty minutes after its passage into the bladder. The amount of dye recovered in the urine was relatively small. In the experiments in which an attempt was made to estimate the dye excreted, only 1 to 2 per cent was obtained in two hours. The concentration of the dye in the bladder seems to be an important factor; and we used a relatively high concentration. No difference was noted between phenolsulphonephthalein and indigocarmine.

TABLE II.—RESULTS OF SERIES OF EXPERIMENTS IN WHICH A MEASURED AMOUNT OF THE DYE WAS INTRODUCED INTO THE BLADDER

| Experiments. | Condition of bladder. | Dye used. | Amount of dye injected, cc. | Appearance of dye. | Apparent amount of dye. | Comments. |
|---|---|---|---|---|---|---|
| 18 | Normal | Phenolsulphonephthalein diluted 1 to 4 with water | 20 | From both ureters in 25 min. | Moderate | |
| 85 | Normal | Phenolsulphonephthalein diluted 1 to 3 with water | 40 | ..... | Trace | |
| 100 | Acute cystitis | Phenolsulphonephthalein diluted 1 to 3 with water | 30 | From right ureter in 30 min.; from left in 60 min. | Large | |
| 875 (1921) | Normal | Phenolsulphonephthalein diluted 1 to 4 with water | 30 | None | None | Injection of the dye into peritoneal cavity; no return; poor secretion of urine. |
| 925 (1921) | Normal | Phenolsulphonephthalein diluted 1 to 4 with water | 45 | None | None | Poor secretion of urine; 1 cc of phenolsulphonephthalein given intravenously; no return. |

In three experiments acutely inflamed bladders were produced by the application of cantharides, a few days before the beginning of the experiment. In two of these experiments the dye was detected in the urine, and in one it failed to appear.

**Discussion.** The urinary bladder is the storage reservoir of an excretion, the elimination of which is of the utmost importance. It would seem, therefore, that the mucosa of the bladder should be more or less impermeable to the passage of the normal contents of the organ. Certainly none of the waste products of metabolism which have been separated from the blood and excreted into the bladder by the kidney should be allowed to reënter the body.

Whether absorption of water which would thus increase the storage capacity of the bladder would be of any advantage is questionable.

The results of our experiments quite definitely prove that a dye can pass through the mucosa of a normal bladder. We were not able to determine whether such absorption takes place primarily through the bloodvessels or lymphatics. The total amount of dye which eventually reaches the blood stream is relatively small. The amount actually absorbed might have been greater than indicated, in view of the fact that all experiments were performed under ether anesthesia which decreases the activity of the kidneys.

The experiments indicate that undoubtedly absorption can take place from the bladder, but that the total amount absorbed is relatively small, and probably has very little practical significance.

That selective absorption of the dyes was a factor in our experiments cannot be denied, but a comparison with the results of other investigators using drugs as the test substance indicates that selective absorption is not a factor.

**Summary.** Extensive investigations on absorption from the urinary bladder present contradictory data. We performed a series of experiments using phenolsulphonephthalein as the test substance. It was found that when the dye was placed in the urinary bladder it appeared in the excreted urine. The total amount excreted was relatively small. These experiments definitely prove that absorption takes place from the urinary bladder, but only to a very limited extent. The contradictory results of previous workers were partially explained.

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## A METHOD OF ESTABLISHING DIABETIC PATIENTS ON HIGH CALORY DIETS WITH A KETOGENIC–ANTIKETOGENIC RATIO WITHIN THE LIMITS OF SAFETY.

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With diabetes, perhaps more than any other disease, set rules for treatment may not be adopted; but general principles based upon a thorough knowledge of the pathological physiology of the disease, if used with critical clinical judgment, are permissible. Such general principles for diabetes have been clearly presented

by Woodyatt,[1] his suggestions being supported by the interesting work of Shaffer.[2 3 4] The discussions of these investigators on the relationship between ketogenic and antiketogenic substances of the diet which is so important in metabolism is full of suggestion for improvement in the diabetic dietary. In metabolism it is convenient to think of the ketogenic substances in terms of fatty acids, and of the antiketogenic substances in terms of glucose; and the studies of Woodyatt and Shaffer so far have shown, for practical clinical purposes, that one molecule of fatty acid is completely oxidized in the presence of one molecule of glucose. Therefore, if in a given diet, the metabolic potentialities for fatty acid do not exceed those for glucose, pathological ketogenesis should not occur. Fatty acid, or perhaps more properly speaking ketogenic potentialities, in metabolism may be derived from fat and from protein; and glucose, or antiketogenic potentialities, from carbohydrate, protein and fat. If these factors are taken into consideration in determining the diet of a diabetic patient, and the entire diet calculated and thought of as fatty acid and glucose only, new possibilities are suggested. Woodyatt[1] has presented formulas for calculating diets along these lines in grams, diets having the proper ketogenic-antiketogenic ratio, and which, by reason of the fat included, afford many more calories without overstepping a low glucose tolerance. The ketogenic value of a given diet is expressed by the formula: $FA = 0.46\ P + 0.9\ F$, in which FA = grams of fatty acid (or ketogenic value of the diet), P = grams of protein and F = grams of fat in the diet given.

The antiketogenic value of a given diet is expressed by the formula: $G = 0.58\ P + 0.1\ F + C$, in which G = grams of glucose (or antiketogenic value of the diet), P = grams of protein, F = grams of fat and C = grams of carbohydrate in the diet given.

The figures upon which these formulas are based are subject to revision by further work, as carefully pointed out by Woodyatt. If one is to know the ketogenic-antiketogenic ratio of food being burned by a patient, however, it is necessary to give a diet which spares his own tissues; for, if he is using his own body tissues, it is impossible to determine accurately the amount of ketogenic or antiketogenic substances being metabolized. Woodyatt, therefore, pointed out the necessity for a diet affording nitrogen equilibrium and, as far as possible, caloric maintenance. The ideal diabetic diet contains then: (1) Enough protein to maintain nitrogen equilibrium; (2) that amount of glucose which the patient has been found able to take without elevation of blood sugar; (3) fat in as large quantities as possible without having the ketogenic-antiketogenic ratio of the diet overstep the limits of safety.

In determining the amount of fat to be given so that there is one molecule of glucose in the diet for every molecule of fatty acid, cognizance is taken of the fact that the average of the molec-

ular weights of the fatty acids from all sources in the diet is 1.5 times as great as that of glucose. Therefore, a diet which contains not more than 1.5 times as many grams of ketogenic fatty acid as glucose is in the proper ketogenic-antiketogenic ratio; and we have:

Potential fatty acid from all sources in the diet,
Potential glucose from all sources in the diet = 1.5 : 1;
or,

$$\frac{FA}{G} = \frac{1.5}{1}.$$

But $FA = 0.46\ P + 0.9\ F$,

and $G = 0.58\ P + 0.1\ F + C$.

Therefore,

$$\frac{0.46\ P + 0.9\ F}{0.58\ P + 0.1\ F + C} = \frac{1.5}{1}.$$

Solving for F (grams of fat to be given in the diet), we have $F = 2\ C + 0.5466\ P$, or in round figures practical for clinical purposes, $F = 2\ C + 0.55\ P$. By substituting in this formula the already known values for the protein and carbohydrate of the diet, the amount of fat to be given is determined.

This conception of the diabetic dietary appeared so hopeful that some months ago, due to the enthusiastic coöperation of Dr. James P. McKelvy, the study of diabetic patients along such lines was begun in the Allegheny General Hospital and the immediate results we are obtaining are very gratifying.

In thinking of the diabetic dietary along the lines suggested by Woodyatt, however, one encounters difficulty from the fact that the glucose tolerance at the beginning is an unknown quantity. To determine this factor by subtracting the amount of glucose excreted from that available to the patient from all sources, while perhaps satisfactory as a starting point, is not entirely so, because the figure arrived at is not the correct glucose tolerance of the patient in many instances. The paper of Felsher[5] is interesting in this connection as contributing experimental data in support of that which has been established by routine clinical observations; namely, the diabetic patient reacts as a normal person to an overstepping of the glucose tolerance by an acute, severe loss of glucose in the urine. For this reason it seemed wise to work out a method of applying the principles outlined above by which the difficulty arising from determinations of the glucose tolerance at the beginning of the study of a case of diabetes might be avoided. This has been done, and so far it has been found convenient and easy in actual practice.

In order to avoid the necessity of determining the glucose toler-

ance, it has been necessary to plan for diabetic patients during the first stages of their study on the basis of their caloric, rather than their glucose, tolerance. Thus, it is our present practice to disregard the glucose tolerance entirely in the beginning of our studies on a case of diabetes and give a test diet having three attributes, differing slightly from those presented by Woodyatt. We demand that our diets: (1) Afford nitrogen equilibrium; (2) afford caloric maintenance as nearly as possible; (3) have a ketogenic-antiketogenic ratio within the limits of safety.

In planning such a diet, two factors are known: (1) The protein to be fed—the number of grams per kilo of body weight found necessary to keep the patient in nitrogen equilibrium; (2) the total calories to be given—the number of calories calculated from the basal metabolism studies, to keep the patient on a caloric maintenance diet.

Knowing the amount of protein to be given, if the carbohydrate were known, the fat can be determined by substituting in Woodyatt's formula $F = 2\ C + 0.55\ P$. To determine the amount of carbohydrate to be given, however, a formula in addition to those already published becomes necessary. Accordingly, we have derived a formula, using the two known factors above (grams of protein and total calories the diet is to contain) which is very simple in derivation and application and has been found practicable. A table has been presented by Holmes[6] for the computation of diets by Woodyatt's formulas; and recently Hannon and McCann,[7] and O'Hara[8] have presented very ingenious charts, by the use of which calculations of diets according to the principles reviewed in this paper are made easy. The formula here presented is for the same purpose and, because of its extreme simplicity and immediately practical features, may also be of use to those who are working with this most interesting conception of the diabetic dietary.

The formula we use for calculating the number of grams of carbohydrate in the diet to be given when the amount of protein and total calories have been decided upon, merely records the fact that each gram of fat produces 9 calories, each gram of carbohydrate 4 calories, and each gram of protein 4 calories; therefore, the number of grams of each of these substances in the diet, multipled by the number of calories afforded by each gram and added together equals the total caloric value of the diet. This, when expressed mathematically becomes $9\ F + 4\ C + 4\ P = Cal.$, in which F = grams of fat, C = grams of carbohydrate, P = grams of protein and Cal. = total calories in the diet given. Substituting in this formula the value for F from Woodyatt, $F = 2\ C + 0.5466\ P$, we have $9\ (2\ C + 0.5466\ P) + 4\ C + 4\ P = Cal.$ Solving for C we get $18\ C + 4.92\ P + 4\ C + 4\ P = Cal.$, or $22\ C + 8.9\ P = Cal.$, and finally $C = \frac{Cal. - 8.9\ P.}{22}$

The use of this formula may best be illustrated by an example: A patient weighs 70 kilos and has been found to need 1 gm. of protein per kilo of body weight to maintain nitrogen equilibrium, and 30 calories per kilo for caloric maintenance. He will, therefore, be given 70 gm. of protein in a diet affording, if he can take it, 2100 calories.

Substituting these values in formula $9\,F + 4\,C + 4\,P = Cal.$, we have $9\,F + 4\,C + 280 = 2100$, or $9\,F + 4\,C = 1820$. Substituting in this the value $F = 2\,C + 0.55\,P$ (from Woodyatt) we have $9\,(2\,C + 38.5) + 4\,C = 1820$, $18\,C + 346.5 + 4\,C = 1820$, $22\,C = 1473.5$, $C = 67$. More simply, by substituting in formula $C = \frac{Cal. - 8.9\,P}{22}$, we have $C = \frac{2100 - 623}{22}$, or $C = 67$.

By substituting the value of protein and carbohydrate determined as above outlined in Woodyatt's formula $F = 2\,C = 0.55\,P$, the fat to be given is found to be 172.5 gm.

The diet to be given the patient in question would then be:

| | Grams. | Calories. |
|---|---|---|
| Protein | 70.0 | 280.0 |
| Carbohydrate | 67.0 | 268.0 |
| Fat | 172.5 | 1552.5 |
| Total | | 2100.5 |

Proving this diet according to the values advanced for present use by Woodyatt, $G = C + 0.58\,P + 0.1\,F$, $FA = 0.46\,P + 0.9\,F$, we have $G = 67 + 40.6 + 17.25 = 124.85$, $FA = 32.2 + 155.25 = 187.45$.

Glucose, or the antiketogenic value of the diet (124.85) multiplied by 1.5 = 187.28. There are, therefore, 1.5 times as many grams of fatty acid—ketogenic potentialities—as glucose—antiketogenic potentialities—in the diet. And the diet thus calculated for a patient, such as taken above, as an illustrative case meets all the specifications we demand, namely: (1) Affords nitrogen equilibrium; (2) affords caloric maintenance; (3) has a ketogenic-antiketogenic ratio within the limits of safety.

If the patient above was found unable to take 2100 calories without an elevation of blood sugar, and it was decided to try him on a diet having 1800 calories, the formula would be $C = \frac{1800 - 623}{22}$; when the diet is solved for this level it would be:

| | Grams. | Calories. |
|---|---|---|
| Protein | 70.0 | 280.0 |
| Carbohydrate | 53.5 | 214.0 |
| Fat | 145.5 | 1309.5 |
| Total | | 1803.5 |

This diet has glucose, or an antiketogenic value—114.7 gm.—and fatty acid, or a ketogenic value—163.2 gm.

The general plan presented above for determining diets for diabetic patients may not be followed to advantage in many cases. Often it is desirable to determine the amount of protein and number of calories to be given by factors other than those suggested. Such variation, however, does not make necessary any change in the formula above, for by substituting the values for protein and calories in the formula as it stands, the amount of carbohydrate to be given may be determined. The two diets worked out above with the same amount of protein have different caloric values. If, for any reason, one desires to change the amount of protein in the diet, while keeping the caloric value constant, the same formula may be used with equal facility for this purpose. For example, if in the first diet above affording 2100 calories it has been found desirable to give 50 gm. of protein instead of 70 gm., the formula would be $C = \frac{2100 - 445}{22}$; when the diet is solved for this combination it would be:

| | Grams. | Calories. |
|---|---|---|
| Protein | 50.0 | 200.0 |
| Carbohydrate | 75.2 | 300.8 |
| Fat | 177.9 | 1601.1 |
| Total | | 2101.9 |

This diet has glucose, or an antiketogenic value—122 gm.—and fatty acid, or a ketogenic value—183.1 gm.

Similarly, if in the second diet above affording 1800 calories, one desires to give 50 gm. of protein instead of 70 gm., the formula would be $C = \frac{1800 - 445}{22}$; when the diet is solved for this combination it would be:

| | Grams. | Calories. |
|---|---|---|
| Protein | 50.0 | 200.0 |
| Carbohydrate | 61.6 | 246.4 |
| Fat | 150.7 | 1356.3 |
| Total | | 1802.7 |

This diet has glucose, or an antiketogenic value—105.7 gm.—and fatty acid, or a ketogenic value—157.6 gm.

Even this early in the work with high-fat diets in diabetes, many considerations not touched upon in this paper have been introduced. For example, Wilder, Boothby and Beeler[9] have shown that the limits of safety of the ketogenic-antiketogenic ratio varies in individuals, possibly directly with the level of the metabolic rate; and Shaffer[10] has shown that a ratio $\frac{FA}{G} = 3/1$ instead of 1.5/1, may in some cases be accompanied by no pathological ketogenesis. A patient who may take safely a diet with a ketogenic-antiketogenic ratio greater than 1.5 : 1 is very rare, however, and unless unusual conditions are present, such feeding is not justified.

Woodyatt[11] is very much in earnest in saying that diets with ketogenic-antiketogenic ratios higher than 1.5:1 should never be employed except when carefully controlled and with a full knowledge of the dangers being courted. To plan such a diet when, if ever, one feels justified in giving it, our formula, with a change in the figures, but not the principle may be used. For example, if $\frac{FA}{G} = 3/1$, then $\frac{0.46\,P + 0.9\,F}{0.58\,P + 0.1\,F + C} = 3/1$ and $F = 5\,C + 2.133\,P$ instead of $F = 2\,C + 0.55\,P$.

Substituting this revised value for F in the formula $9\,F + 4\,C + 4\,P = Cal.$, and solving for C we get $C = \frac{Cal. - 23.2\,P}{49}$.

In Table I appear values for F (grams of fat in diet) for different ketogenic-antiketogenic ratios, and our formula with the figures resulting by using in its derivation these different values for F.

TABLE I.

FA = Fatty acid, or ketogenic potentialities.
G = Glucose, or antiketogenic potentialities.
F = Grams of fat in diet.
C = Grams of carbohydrate in diet.
P = Grams of protein in diet.
Cal. = Number of calories in diet.

| Ketogenic-antiketogenic ratio. | Value for F. | Formula for calculating carbohydrate in diet when amount of protein and number of calories are known. |
|---|---|---|
| $\frac{FA}{G} = 1/1$ | $F = 1.25\,C + 0.15\,P$ | $C = \frac{Cal. - 5.4\,P}{15.3}$ |
| $\frac{FA}{G} = 1.5/1$ | $F = 2\,C + 0.5466\,P$ | $C = \frac{Cal. - 8.9\,P}{22}$ |
| $\frac{FA}{G} = 2/1$ | $F = 2.857\,C + P$ | $C = \frac{Cal. - 13\,P}{29.7}$ |
| $\frac{FA}{G} = 2.5/1$ | $F = 3.846\,C + 1.523\,P$ | $C = \frac{Cal. - 17.7\,P}{38.6}$ |
| $\frac{FA}{G} = 3/1$ | $F = 5\,C + 2.133\,P$ | $C = \frac{Cal. - 23.2\,P}{49}$ |
| $\frac{FA}{G} = 3.5/1$ | $F = 6.364\,C + 2.851\,P$ | $C = \frac{Cal. - 29.7\,P}{61.3}$ |
| $\frac{FA}{G} = 4/1$ | $F = 8\,C + 3.72\,P$ | $C = \frac{Cal. - 37.5\,P}{76}$ |

Used in this manner, this simple formula makes possible the rapid and easy calculation of high calory diets with any ketogenic-antiketogenic ratio, containing any amount of protein, and afford-

ing any number of calories ever to be desired in the diabetic dietary. By its use, diets for diabetic patients, according to the principles emphasized recently by Woodyatt and Shaffer, may be calculated without knowing the glucose tolerance. And if patients are studied at first on the basis of their caloric, instead of their glucose tolerance, a method for the study of the diabetic dietary is available by which the difficulty of determining accurately the glucose tolerance early in the study of the case is avoided.

The details of application of this method of procedure have not been presented, but will appear later in a clinical report of the cases studied. It is hardly necessary to say that this, or any other suggestion, may not be employed as a routine procedure for all cases, or used blindly and unintelligently in any case. It should, perhaps, be emphasized that we present it for use only as a method of procedure in establishing diabetic patients on their maximum food combinations when they have been brought to the stage where this is in order. For this purpose it has been found convenient and practical, and has rendered much more simple the applications of the principles of diabetic feeding outlined above.

**Summary.** Following upon the recent studies of Woodyatt and Shaffer on the ketogenic-antiketogenic ratio in metabolism, and the practical application of these studies for establishing diabetic patients on a high-calory diet, a conception of the diabetic dietary, based primarily on the caloric, rather than principally upon the glucose tolerance of the patient, is presented; and a simple formula for the necessary computations is derived. This method of procedure is helpful because it enables one to study diabetic patients without first establishing the glucose tolerance, which is so difficult to determine accurately. The early results obtained by this method of feeding diabetic patients have so far been extremely gratifying.

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# MEDICAL TREATMENT OF GASTRODUODENAL ULCER, WITH ESPECIAL REFERENCE TO THE USE OF A RICE-WATER MIXTURE.*

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Much has been written about gastric ulcer, or, if you please, peptic ulcer, and much has been suggested by way of treatment for this perplexing lesion. Medical measures claim a high percentage of therapeutic triumphs as a result of their practice, while the surgeon puts forth splendid statistics to show the efficacy of his scalpel. Each of these opposing camps claims failures on the part of the other. The medical man points to the surgical derelicts he has had to care for and the surgeon calls attention to the innumerable times he is called upon to rescue the medically treated patient or perhaps, what is more to the point, his doctor. The literature is filled with many suggestions for the non-surgical care of these cases, while an almost equal amount of space is devoted to the best non-medical technic to follow. The treatment of gastroduodenal ulcers is, in other words, not universally satisfactory.

When a multiplicity of suggestions are made for the relief of any disease, ordinarily none of the methods are actually effectual. This does not seem to be true of ulcer cures, for the relationship of cause and effect is usually in this connection a clear-cut one. Sometimes uncertain etiology makes for a varied therapeusis. This too does not seem to be the case here, even though the cause of ulcer is not certainly settled. Obviously many methods of handling ulcers medically or surgically are recommended because of the many changing indications to be met with in these cases. For example, the problem of the chronic cicatrized ulcer is quite apart from that of the earlier gastric lesions and, therefore, must require different care.

Lack of success in the treatment of gastroduodenal ulcer is dependent for the most part upon a failure to appreciate these changing therapeutic indications. Variable results are reported when the same method of treatment is applied in all cases; failures would of necessity follow such a practice. Often, of course, conditions do not permit thorough application of the indicated treatment in a given patient, a circumstance which does not allow for a uniformly successful outcome. Sometimes, in the interests of time economy, surgery is practised when a right sort of medical regimen would have done better. On the other hand, quite fre-

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quently a medical cure is quite impossible in the presence of very advanced pathology. Surgery promises quick results, but a careful analysis shows that this speed is more apparent than real. The post-surgical ulcer case requires, as a rule, a long period of good medical care if lasting effects are to be accomplished. Here, as elsewhere, a big opportunity for practice, with attention to early diagnostic and therapeutic detail, makes for successful results, while inexperience and short cuts often spell failure. Almost every one has some particular treatment with which he is especially familiar. Every method of handling ulcers therefore has its champions and critics.

All suggested medical treatments require time, and are usually complicated, necessitating much thought and detailed attention. Casual practice of this method is therefore doomed to meet with many ulcer failures. Rest of the mind and body, but more particularly of the stomach, is a part of medical treatments in general. Bed rest and preliminary degrees of starvation are usually suggested with provisions made for enematization or the introduction of fluids into the body by hypodermoclysis. The suggested diets generally provide for small fractional feedings of bland, non-irritating food at frequent intervals. Medical men are more or less divided as to whether or not the diet should be purely carbohydrate or protein. Some few combine both types of foods. The list includes milk, eggs, broths, gruels, starch solutions and other articles too numerous to mention. The carbohydrate enthusiasts feel that proteins, instead of diminishing, stimulate an overproduction of gastric juice, while the proponents of the latter diet contend that it serves to combine with the free acid and thereby minimizes its digestive action upon the ulcer. The fact of the matter is that the use of both diets is followed by successes and failures. At times this, and at times another diet or scheme succeeds. Sometimes a medical treatment should not even be attempted. Feedings by transduodenal intubation often yield gratifying results. It is part of all treatments to first of all seek out infective foci in the body and then attempt to erase them. The relationship of ulcer to focal infection is now upon quite certain ground. Medicines used in conjunction with diets usually aim to influence hyperfunctionation of the stomach whether this be of motility, secretion, or sensation. They are chiefly concerned in the neutralization of the free acid. Other medication is often employed to reduce gastric irritability. In this way nerve sedatives and antispasmodics play an important role in many medical treatments. Drugs must also be employed quite frequently to hurry the intestinal transportation of the unusually non-stimulating and scanty food residue. Hydro-mechano-electrotherapeutic procedures occupy a large place in most of the ulcer regimens.

Granting that the case is not accompanied by high-grade cicatrized pyloric obstruction, that there is no perforation or that carcinomatous implantation is not a reasonable possibility, that there is no perigastric abscess or hour-glass contraction, and that there are no unusual perigastric adhesions, then variously suggested medical treatments can be tried. All of them, however, usually emphasize hospitalization or at least bed treatment. Most textbooks and literature in general devote much space to a strict rest treatment of ulcer with an occasional reference to the possibilities of ambulatory treatment. Sometimes the patient's social or financial status will not permit bed treatment, to say nothing of hospital care. Sometimes the patient's mental attitude is contradicatory to this mode of treatment. At times surgical treatment is not acceptable to the ulcer victim, and at other times the surgeon may suggest a preliminary trial of medical measures. What can be tried in these events? What are the therapeutic possibilities in the patient coming to the out-patient department? Surely these cannot be thrust aside untreated.

All of the well-known treatments can be applied with certain modifications to the average ambulatory case. Hourly feedings can be arranged for with little difficulty. Usually thirteen a day are suggested, but sometimes two-hour intervals serve equally well. Women working at home can of course easily provide themselves with the necessary diet, while the working man or working woman can carry enough food in thermos bottles or the ordinary magnesium citrate bottles. Many cases can be started on a milk and cream combination after the Sippy method, using of course adequate amounts of calcium carbonate, bicarbonate of soda and magnesium oxide between feedings. If the patient tends toward constipation the amount of magnesium oxide taken is increased, while the looseness of the bowels is a signal for an increased intake of calcium carbonate or even the addition of bismuth subcarbonate. Lime water or sodium citrate, 0.6 gm. may be added to each one of these milk and cream feedings. Sodium citrate seems to lessen the irritability of the milk curd. At night or at some time out of working hours, hot-water bags, ice bags, poultices, or tincture of iodine may be applied to the epigastrium for varying periods of time. The gastric retention cases can be trained to empty their stomachs at night with the stomach or, better still, the duodenal tube.

There are always a number of cases in whom the milk and cream regimen does not promptly arrest pain or other symptoms. In these cases we have found a rice-water mixture used by Dr. Joseph Sailer, of Philadelphia, to be of very great value. In our outpatient department[1] a patient is given a printed slip of paper con-

[1] Gastrointestinal Division, Outpatient Department, Hospital of the University of Pennsylvania.

taining the following information and suggestions with supplementary explanations by the dietitian:

RICE-WATER FORMULA.

Boil one-half cup of rice in five cups of slightly salted water until soft. Strain off and cool one quart of the water. When cool add to it four tablespoons of lactose, whites of four eggs, slightly beaten, and one-half cup of cream. Keep the mixture in a cool place.

Take_____of the mixture every hour throughout the day, until thirteen feedings have been taken.

Secure a bowel movement each day. If necessary use milk of magnesia for this purpose.

Take note of weight and report back after_____days. Lactose is milk-sugar and may be purchased at any drug store.

The palatability of the rice-water mixture may be influenced by the addition of peppermint, chocolate, nutmeg, or coffee. It is a difficult matter to accurately determine the caloric value of this mixture, but it is quite likely that a quart will yield at least 750 calories. Two to six-ounce portions of this preparation are usually taken at hourly intervals for thirteen feedings per day. There are, of course, cases who are advised to take the mixture at two-hour or even longer intervals. After the symptoms are allayed for twenty-four hours at least, the caloric value of the rice-water mixture is increased by adding more cream, sugar or whites of eggs. Very quickly after this the patient goes on to either a partial or entire milk and cream mixture and, if well tolerated, passes on to a soft or light diet, usually preponderant carbohydrate.

In addition to the mixture we frequently employ some one of the antacid preparations. Another favorite procedure is to prescribe after the first, seventh and thirteenth feedings and at bedtime a teaspoonful of the popular nux, soda and gentian mixture of our hospitals. To this prescription we may add sodium bromide 0.3 to 0.6 gm., and sometimes, if required, a variable amount of the fluid extract of rhamnus purshiana.

It is most gratifying to note the rapidity with which symptoms disappear when this mixture is prescribed. Many patients are given this diet in a tentative way while in the course of study. Frequently nothing else is required. The neurosis cases, with the exception of the aërophagics, do especially well under this regimen, when quite frequently they object to other milk mixtures. In the functional cases we sometimes use a powder containing 0.3 gm. each of sodium bromide, carbolignum, calcium carbonate and magnesium oxide. All patients are impressed with the fact

that strict adherence to instructions is required for success. They are reminded that successful gastric therapeusis means months and somtimes years of attention to self-care and self-control in matters of diet. They are also impressed with the necessity of securing a bowel movement each day. They are advised to observe their weight and report back if there is much loss in this direction. Of course, every effort is made to maintain the patient's weight, usually by increasing the caloric value of the mixture.

If the history, physical examination, test-meal and roentgen-ray studies point to an ulcer diagnosis, this rice-water treatment seldom fails to relieve symptomatically, and in time we believe pathologically. The use of this mixture has now been observed over a period of time and in a sufficient number of cases of varying types to enable one to say that it meets most satisfactorily the problem of the gastric irritability syndrome both without and, more especially, with ulcer. If it fails to relieve we have usually found our diagnosis to be incorrect or that we are dealing with a case indicating surgery.

We have even observed twenty-four-hour pyloric obstruction cases return to almost normal gastric motility in several weeks on this rice-water ambulatory regimen; of course, this, too, has been our experience with the Sippy method as well. The subperforation or adhesion cases do not yield very readily to any medical treatment. The type adherent to the pancreas have been especially difficult to deal with. Even the surgeon is content with only a gastrojejunostomy in these patients. In patients who have not had roentgen-ray studies, failure of the rice-water mixture to relieve symptoms strongly indicates the use of this diagnostic measure. Very occasionally the rice-water mixture succeeds in a bed treatment when it has failed in ambulatory treatment. Its best results are obtained in the cases accurately diagnosed in early stages. Early diagnosis is just as desirable here as in other fields of medical endeavor. The rice-water mixture is easily prepared and kept. Many patients obtain such great relief that it is difficult to persuade them to go on to more complex food.

**Summary.** 1. Attention is called to some reasons why variable results are reported in gastroduodenal ulcer treatment.

2. Reasons for therapeutic failures are noted.

3. The general plan of medical treatments is reviewed.

4. The possibility of ambulatory treatment in peptic ulcer is reëmphasized with some directions for cases in whom it is the only alternative.

5. The satisfactory use of a rice-water mixture in the gastric hypersyndrome, more especially with ulcer, is suggested.

6. Claim is made for this mixture that, although it adds another diet to the already crowded field of ulcer therapeusis, in our experience, it has tended more to simplify than complicate the problem of treating gastric irritability.

# THE STABILITY OF ADRENALIN HYDROCHLORIDE IN VARIOUS SOLUTIONS.

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The active principle of the medullary portion of the suprarenal glands, properly designated as epinephrin, has become so widely known under its trade name, that it will be referred to as adrenalin in the present article.

Before the active principle of the suprarenals had been isolated in pure form and its formula determined, it was recognized that it was readily destroyed by oxidizing agents. It was learned, moreover, that this oxidizing action was accelerated by an alkaline reaction, while it was prevented, or markedly retarded, by even a slight degree of acidity. The lability of the substance is appreciated by the manufacturers of adrenalin who state on the labels of the bottles that chloretone and carbonic acid are added in order to prevent deterioration. They also point out that simple dilution in salt solution gives rise to a rapid loss in pressor action of adrenalin. They have not emphasized, however, that the addition of alkalies is apt to hasten deterioration; and we have found that local physicians who prescribe adrenalin for its constrictor action in the nose and throat are apparently unaware that this desired action may fail to be elicited because of the nature of the vehicle in which the drug is exhibited.

Investigation in the dispensary of the Medical College of Virginia has shown that the following vehicles are frequently used in conjunction with adrenalin: Glycothymoline; borolyptol; alkaline antiseptic solution, N.F.; Dobell's solution; listerine; and normal saline. It was decided, therefore, to ascertain the keeping qualities of adrenalin in these various solutions.

Solutions of adrenalin were prepared, in the strength of 1 to 100,000, in each of the preceding diluents. The pressor action of these solutions was determined at the time they were made up by ascertaining the effect they were capable of producing on the blood-pressure of a dog. The animals used in these experiments were either anesthetized by the intracerebral injection of magnesium chloride, or they were decerebrated. In all instances the vagi were cut in the neck to avoid the inhibitory action of adrenalin on the heart, and artificial respiration was employed. The injections were made into the femoral vein and the carotid blood-pressure

was recorded by a mercury manometer. The dose selected was 0.5 cc of the 1 to 100,000 solution per kilogram of body weight.

Since the circulatory effects of adrenalin under the conditions described are evanescent, it was possible to compare the relative strength of a number of different preparations on any one dog. In order, however, to obtain information as to the keeping qualities of the solution, it was necessary, obviously, to make use of a number of different animals on succeeding days. In carrying out these later experiments, in addition to comparing the different solutions with each other, their pressor action had to be compared with that of a standard prepared by diluting a small amount of the stock solution in physiological saline.

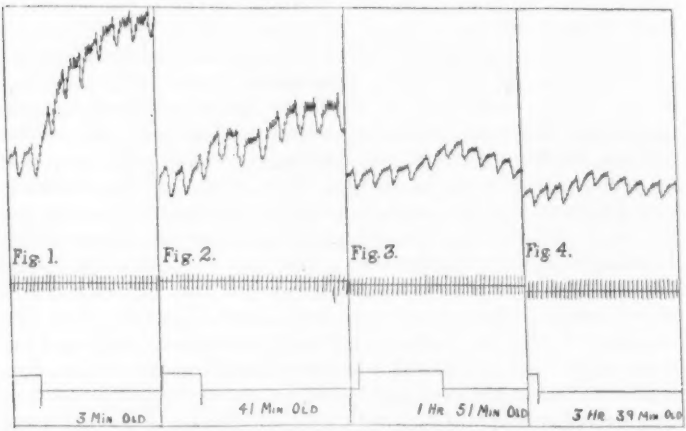


CHART I.—Adrenalin hydrochloride 1 to 100,000; 0.5 cc per kg. in borolyptol. Fig. 1, three minutes old; Fig. 2, forty-one minutes old; Fig. 3, one hour and fifty-one minutes old; Fig. 4, three hours and thirty-nine minutes old.

The results of these experiments were surprising in indicating how rapidly adrenalin was destroyed in certain of the commonly used vehicles. Thus, the dilution in borolyptol was found to be practically devoid of any pressor action at the end of a little over three hours and a half. The tracings in Chart I, all obtained from the same dog, illustrate in a striking manner the progressive and rapid loss of strength of the adrenalin in this vehicle. The stability of adrenalin in glycothymoline is only slightly greater than it is in borolyptol. Thus, at the end of three hours and forty-one minutes there had been a decided loss in activity, while twenty-four hours later there was no evidence of any constrictor action (Chart II). In Dobell's solution there was a distinct loss of activity at the end of twenty-four hours (Chart III) and the preparation was found to be inert at the end of a week. Since

these three vehicles are all alkaline in reaction, a destruction of adrenalin is to be expected when it is dissolved in one of them. It is evident that the addition of adrenalin to borolyptol or glyco-

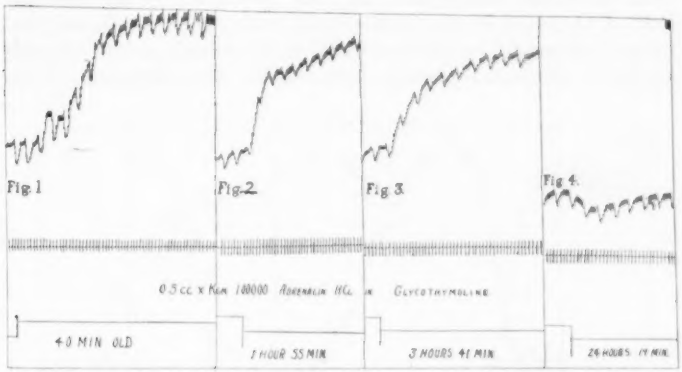


CHART II.—Adrenalin hydrochloride 1 to 100,000; 0.5 cc per kg. in glycothymoline. Fig. 1, forty minutes old; Fig. 2, one hour and fifty-five minutes old; Fig. 3, three hours and forty-one minutes old; Fig. 4, twenty-four hours and nineteen minutes old.

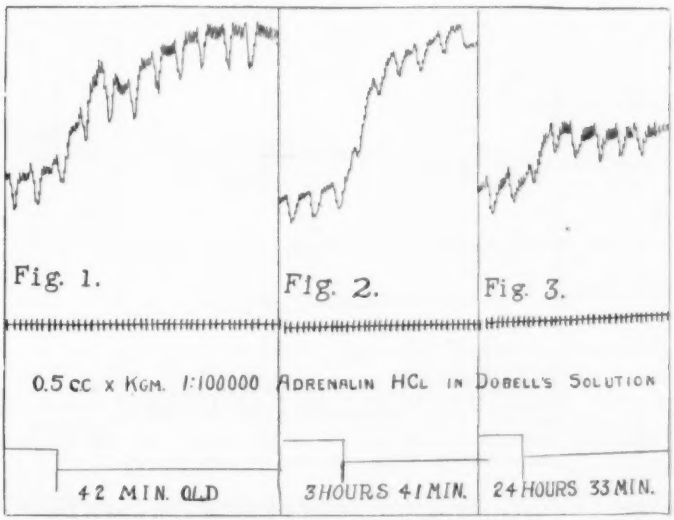


CHART III.—Adrenalin hydrochloride 1 to 100,000; 0.5 cc per kilogram in Dobell's solution Fig. 1, forty-two minutes old; Fig. 2, three hours and forty-one minutes old; Fig. 3, twenty-four hours and thirty-three minutes old.

thymoline is practically useless, so rapid is the oxidation of the amine. Even in Dobell's solution one could expect no constrictor action from the adrenalin at the end of a week.

Williams and Sweet have recently called attention to the fact that the reaction of physiological salt solution is not necessarily neutral and constant. They showed that such solutions gradually tend to become somewhat acid from absorption of the carbonic acid of the air. In our experiments with saline we found that adrenalin in a dilution of 1 to 100,000 in 0.9 per cent sodium chloride was more stable than in the three vehicles first discussed. After

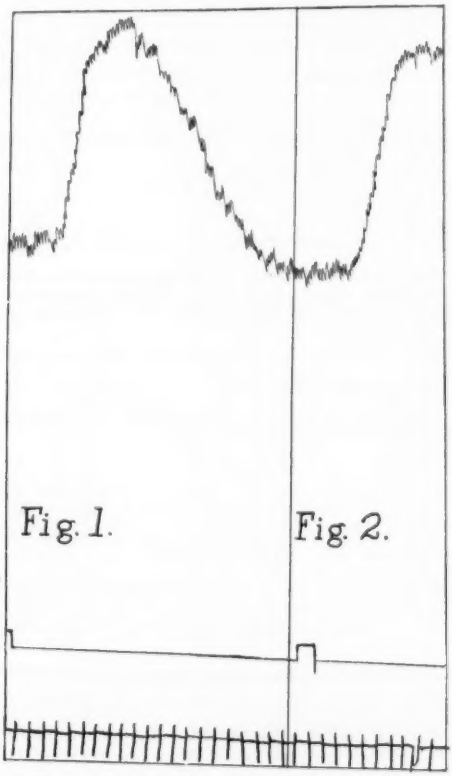


CHART IV.—Adrenalin hydrochloride 1 to 100,000; 0.5 cc per kg. Fig. 1, in fresh saline solution; Fig. 2, in listerine, nineteen days old.

a month there was little or no loss of pressor action and it became inert only after fifty-nine days. We were possibly in error in assuming that our salt solution was neutral, as no determination of its hydrogen-ion concentration was made. Such results with saline cannot be widely applied because, as has been explained, various specimens of saline may behave differently, and it is quite possible that the one with which we have been experimenting had

acquired a certain degree of acidity. Incidentally, it should be noted that the addition of small amounts of antipyrine to adrenalin in salt solution causes a relatively rapid loss of pressor action to the solution.

Listerine and the plain antiseptic solution of the N.F. are both slightly acid in reaction, due to their content of benzoic acid and boric acid respectively. Our early experiments indicated that the

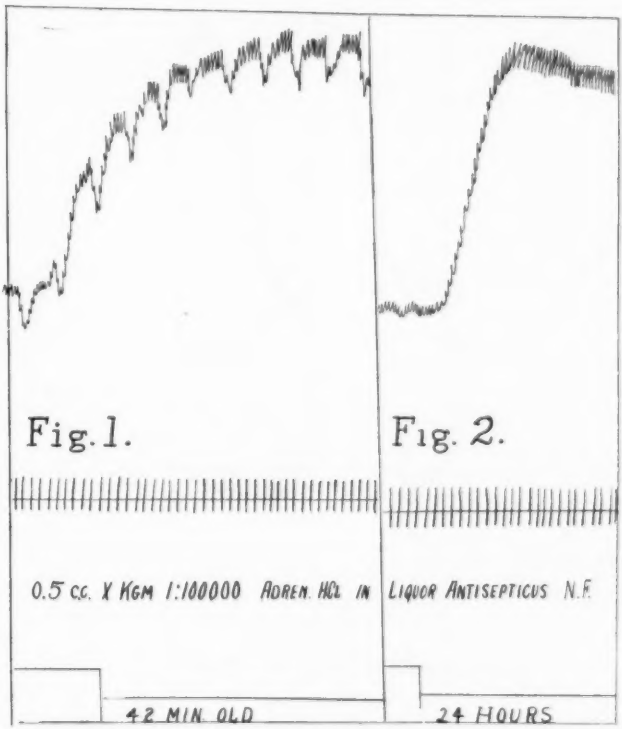


CHART V.—Adrenalin hydrochloride 1 to 100,000; 0.5 cc per kg. in plain liquor antisepticus, N. F. Fig. 1, forty-two minutes old; Fig. 2, twenty-four hours old.

solutions of adrenalin in these vehicles preserved the pressor action remarkably well. Thus it was found that adrenalin in listerine was fully as active as the freshly prepared standard at the end of nineteen days (Chart IV). The solution of adrenalin in the plain antiseptic solution, N.F., was similarly stable (Chart V), and we have found no appreciable loss of strength at the end of four months.

The next step was to determine whether the benzoic acid present in listerine is, of itself, sufficient to manifest this preservative

action. Accordingly, solutions of adrenalin were made up in the strength of 1 to 100,000 in both 0.2 per cent and 0.02 per cent benzoic acid. The subsequent testing of these solutions revealed that the

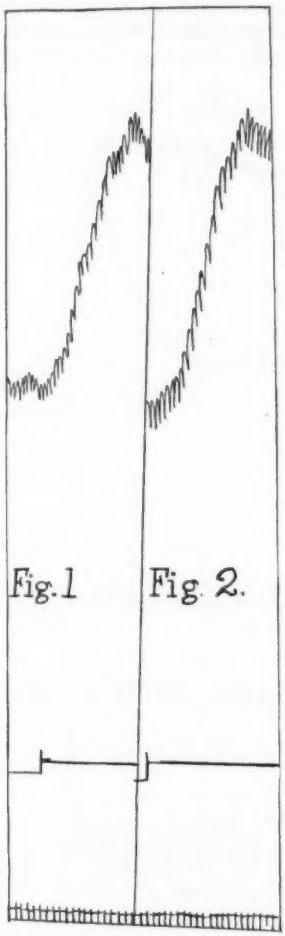


CHART VI.—Adrenalin hydrochloride 1 to 100,000; 0.5 cc per kg. Fig. 1, fresh saline solution (standard); Fig. 2, benzoic acid, 0.02 per cent, nineteen days old.

benzoic acid was quite effective, there being no evidence of loss of pressor activity at the end of nineteen days, even in the weaker concentration (Chart VI). In the strength of 0.2 per cent benzoic acid the solution was very stable, losing only about 15 per cent of

its constrictor action in fifteen months. Even in the strength of 0.02 per cent benzoic acid, about 33 per cent of the pressor action was manifest at the end of fourteen months (Chart VII).

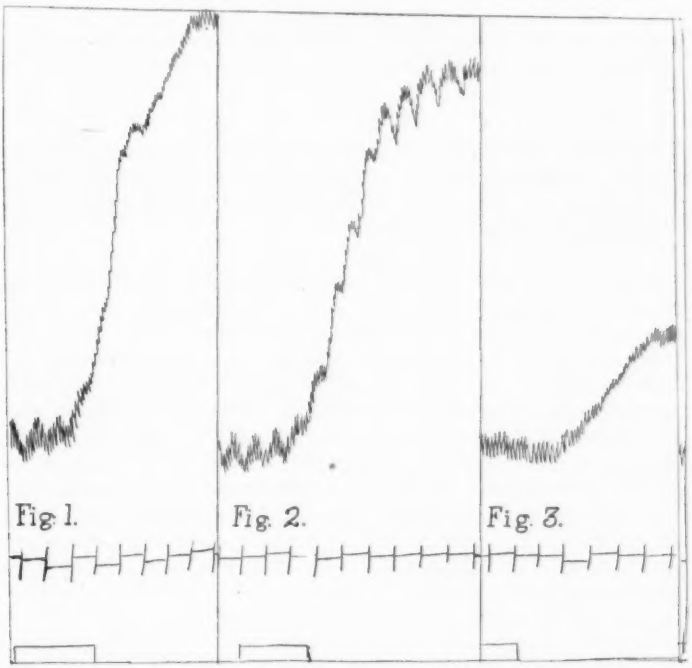


CHART VII.—Adrenalin hydrochloride 1 to 100,000; 0.5 cc per kilogram. Fig. 1, fresh saline solution (standard); Fig. 2, benzoic acid, 0.2 per cent, fifteen months old; Fig. 3, benzoic acid, 0.02 per cent, fourteen months old.

**Conclusions.** As a result of the above experiments we would suggest that adrenalin may be prescribed in normal saline in cases where prompt utilization is intended. If, however, the pressor activity of the adrenalin is to be preserved for any length of time, we would recommend its dilution in a weak solution of benzoic acid. Whether the demonstrable stability of adrenalin in such a solution is due to some action of the benzoic acid *per se*, or due simply to the hydrogen-ion concentration of the solution, we are not prepared to say, but we are now engaged on further experiments to determine this point. Our investigations demonstrate graphically the utter uselessness of prescribing adrenalin in solutions which have an alkaline reaction.

# REVIEWS.

I Believe in God and in Evolution. By William W. Keen, M.D., Emeritus Professor of Surgery, Jefferson Medical College, Philadelphia. Pp. 100; 3 illustrations. Philadelphia: J. B. Lippincott Company, 1922.

Here is the credo of a great man simply stated for any who care to read sympathetically. The author is distressed that others cannot see the unity of the divine plan as clearly as he does. He believes in God and in evolution and this little book evidently has been written in the hope that by restating the matter in almost primer language some, who now see the theory of evolution and the Christian religion as antagonistic, may be brought to the opposite view. There is nothing controversial in the book, there is nothing so scientific as not to be understood by any reader. It is a book rather for one who, untrained in science and ignorant of the facts upon which the theory of evolution is founded, yet believes in Christianity. It cannot fail to carry a convincing message to all whose minds are other than closed. P.

What To Eat in Health and Disease. By Benjamin Harrow, Ph.D., College of Physicians and Surgeons, Columbia University. Pp. 195; 17 illustrations. New York: E. P. Dutton & Co., 1923.

This book, by the author of "Vitamines, Essential Food Factors," etc., is, as the preface states, a guide for those who want to know what to eat and why. Written for popular use, it puts a scientific knowledge of foods into everyday language, with quotations from the sources, and references for further study. There are chapters, among others, on the planning of meals, the nursing mother, infant feeding, vegetarianism, overweight and underweight, constipation, etc. The relationship of diseases and diet is clearly set forth, and there is a final chapter on the chemistry, physiology and anatomy of the digestive tube. For the patient who wishes to follow intelligently the directions of his physician, this will prove a very helpful book. McC.

RADIUM BIBLIOGRAPHY AND ABSTRACTS OF SELECTED ARTICLES ON RADIUM AND RADIUM THERAPY. Compiled by American Institute of Medicine for United States Radium Corporation, New York. Pp. 132 and 164. New York: 1922.

THE bibliographical pamphlet presents in 15 sections several thousand references on the use of radium and results obtained from its discovery up to January, 1922. In each section the titles are arranged by year of appearance, the most recent years appearing first. This collection should prove a useful addition to a working library, although it is far from complete, especially in non-clinical lines. The literature before 1903, is particularly meager and one misses the pioneer articles of Becquerel and the Curies. The pamphlet of abstracts is even more restricted, but will doubtless be welcomed by radiotherapeutists. K.

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HANDBOOK OF ELECTROTHERAPY. By BURTON BAKER GROVER, M.D.; President of the Western Electrotherapeutic Association; Member of the Radiological Society of North America, etc. First edition. Pp. 420; illustrated with 103 engravings in the text and 6 plates of 12 charts. Philadelphia: F. A. Davis Company.

THE last few years have witnessed a number of new volumes written on this same subject of electrotherapy. The book covered by this review discusses very completely all phases of the subject beginning with the fundamental principles of electricity. Chapters are included on high blood-pressure, hyperpiesis, genito-urinary diseases and a whole host of other conditions said to be amenable to electrotherapeutic procedure.

The style is exceedingly simple. It would seem that the author in his endeavor to achieve simplicity of style has often sacrificed accuracy of statement from the clinical standpoint. From the electrotherapeutic side, Grover is naturally hyperenthusiastic, just as all are who are engaged in this work. There is, of course, a group of medical men who are too skeptical concerning the efficacy of this branch of therapeutics. The middle ground seems a more tenable one, namely, that there are many functional conditions which are very favorably influenced by electricity and indeed there are some organic lesions in which therapy of this sort seems to make the patient more comfortable.

One would prefer to read less of Abrams and his methods. A suggested addition to the value of such a book would be the inclusion of statistical records with accurate follow-ups of a large series of cases treated by electrotherapeutic measures. If such statistics,

honestly made, would show that electricity uniformly does influence favorably all the diseases covered in this volume, then we would be in accord with the spirit of the author. The writer in the preface justly calls attention to the fact that little opportunity is given to medical men as undergraduates to become familiar with modern methods of electrotherapeutic application. It does seem fair to say that our medical schools should emphasize this branch more than they are in the habit of doing. It is quite possible that there would be more converts to this field as a result of more successful results and that there would be fewer practitioners of the various cults. S.

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STUDIES IN THE STANDARDIZATION OF THE WASSERMANN REACTION WITH THE DESCRIPTION OF A NEW METHOD. By JOHN A. KOLMER, M.D., Professor of Pathology and Bacteriology in the Graduate School of Medicine of the University of Pennsylvania, and Head of the Department of Pathology in the Research Institute of Cutaneous Medicine of Philadelphia; assisted by C. P. BROWN, T. MATSUNAMI, A. M. FLICK, A. RULE, M. E. TRIST, and E. YAGLE. Pp. 580; 7 illustrations. Philadelphia: 1923.

IN this volume the reprints of one publication appearing in the AMERICAN JOURNAL OF MEDICAL SCIENCES, and those of thirty-two publications appearing in the American Journal of Syphilis during the years 1919 to 1922 are collected. These publications represent an extensive experimental investigation of the values of the more plausible of the many technical modifications suggested in antecedent literature on the technic of the Wassermann test. The modifications shown to be of greatest worth are utilized in building a method for the conduct of the test. S.

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TEXT-BOOK OF PEDIATRICS. Edited by Prof. E. FEER, Director of the University Children's Clinic, Zurich; translated and edited by JULIUS PARKER SEDGWICK, B.S., M.D., Professor of Pediatrics, University of Minnesota, Medical School; and KARL AHRENDT SCHERER, M.D., F.A.C.P. Pp. 917; 262 illustrations. Philadelphia and London: J. B. Lippincott Company, 1922.

SEVENTEEN American pediatricians have translated the seventh edition of the author's well-known book on pediatrics. The character of the work performed by the American collaborators is of a very high order, and additions have been made both to

text and illustrations. No attempt has been made to describe in detail diseases discussed at length in the general text-books on medicine, but measles, pertussis, varicella, and nutritional disturbances are dealt with in especial detail. The book is up to date, and can be recommended without hesitation to the general physician as well as to the pediatrician. A.

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AN INDEX OF PROGNOSIS AND END-RESULTS OF TREATMENT. By VARIOUS AUTHORS. Third edition. Pp. 594. New York: William Wood & Co., 1922.

As our treatment of various diseases improves, the prognosis becomes more favorable; therefore, constant revision of any work on prognosis is required. The present volume reflects the better prognosis offered by the more modern methods of treatment of epithelioma of the lip, strangulated hernia, and intussusception. The sections on venereal diseases, gynecology, and obstetrics have also been rewritten, and a new section on ophthalmology has been contributed.

Those who desire to find a brief discussion of medical and surgical diseases, with special reference to prognosis, will be pleased with the book; however, the work will still be a disappointment to those who are awaiting a scientific statistical study of the probability of death or disability, and the expectancy of life in each disease. A.

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IMPOTENCY, STERILITY, AND ARTIFICIAL IMPREGNATION. By FRANK P. DAVIS, PH.B., M.D. Second edition. Pp. 163. St. Louis: V. C. Mosby Company, 1923.

A CAREFUL reading of this book has failed to convince the reviewer of its value as an addition to his library. The first one hundred and ten pages are a hazy, Freudian discussion of such topics as sensuality in women, the effect of odors on internal secretions, and the influence of the senses of smell, sight and hearing in impotency.

The directions for treatment of sterility and impotence include suggesting that the woman sing at the top of her voice during the copulative act as a sure remedy for sterility, and that Chinese incense burned in the room gives off an odor that excites sexual power and desire.

The author loans sterile couples a speculum and a syringe in order that they may practice artificial impregnation at their convenience. Such a proceeding may be questioned. It is difficult to understand the necessity for this second edition. W.

STERILITY IN WOMAN; ITS CAUSES AND TREATMENT. By ROBERT A. GIBBONS, M.D., M.R.C.P., C.M., F.R.C.S.E., Gynecologist to the Grosvenor Hospital for Women. Pp. 219; 44 illustrations. London: J. and A. Churchill, 1923.

THIS monograph is a detailed study of the subject, written in a clear and interesting manner by one well informed on his subject. Statistics may or may not be misleading but a reading of the first chapter on Sterility and the State shows how important a problem is under discussion. The following four chapters are on the Physiology of Conception, Structural and Functional Causes and Medical and Operative Treatment. The single omission of note is the absence to any reference to trans-uterine insufflation of the Fallopian tube (Rubin's test). In all other respects, however, the book is fully abreast of the most recent literature on the subject.

W.

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A HISTORY OF MAGIC AND EXPERIMENTAL SCIENCE DURING THE FIRST THIRTEEN CENTURIES OF OUR ERA. By LYNN THORNDIKE, PH.D., Professor of History in Western Reserve University. In two volumes. Pp. 835 and 1036. New York: Macmillan Company, 1923.

THE medical man who is interested in the history of medicine will find these two volumes of great value not only as reference books but also to give him a broad knowledge of early attempts at scientific work up to the Fourteenth Century. He will find before him a book which deals in a most complete, and thorough manner with early experimental science and what is also most interesting, with early magic. The work is divided into two volumes and five books. The first volume contains three books: (I) The Roman Empire; (II) Early Christian Thought; (III) The Early Middle Ages; while Volume II contains books IV and V on The Twelfth Century and the Thirteenth Century. In going over the book in a non-critical way, the reviewer is struck with the clear exposition of the subject, the delightful methods of presentation used by the author and the undoubted authoritativeness of the material. The influence of Roger Bacon and the importance of his contributions to science in the Thirteenth Century may be exemplified by the importance the author lays upon his work, devoting nearly eighty pages to the life and works of this wonderful man. Celsus is also thoroughly gone into and, to our English confrères who are obliged to read Celsus before they can go up for their final examinations, this admission to the text of a complete discussion of Celsus's work will seem eminently proper.

M.

SYMPTOMS OF VISCERAL DISEASE. A Study of the Vegetative Nervous System in its Relationship to Clinical Medicine. By FRANCIS MARION POTTENGER, A.M., M.D., LL.D., F.A.C.P., Medical Director, Pottenger Sanatorium for Diseases of the Lungs and Throat, Monrovia, California. Second edition. Pp. 357; 86 illustrations and 10 color plates. St. Louis: C. V. Mosby Company, 1922.

THE present interest in the physiologic aspect of clinical medicine and the uniqueness of Dr. Pottenger's contributions along the line of functional visceral neurology in the explanation of symptoms are undoubtedly the reasons for the ready appearance of a second edition of his book. As implied in this Journal's review of the original edition, it fills a distinct need in correlating much data in a field that is new to those who have not followed carefully the work of Mackenzie, Head and others. Considerable new material has been added. The illustrations are excellent. While it is true, as has been stated in criticisms of the work, that the terms used, such as viscerogenic, visceromotor, viscerosensory, and viscerotrophic are somewhat cumbersome, yet they are descriptive and for that reason helpful in clarifying a subject that is by no means simple.

The reviewer approves of the attempt to interpret certain symptoms in terms of vegetative nervous system disturbance and believes that Dr. Pottenger's studies in this field will be of great benefit to clinicians and teachers, but he cannot escape the feeling that some of the explanations offered are founded on, as yet, not sufficiently well established facts; for instance, the claim that magnesium sulphate solution when introduced into the duodenum dilates the bile duct sphincter and contracts the gall-bladder (which has not been proved) and that this results from vagus inhibition or sympathetic stimulation (again not proved).

M.

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THE MEDICINE MAN. By JOHN LEE MADDOX, PH.D., Captain (retired), U. S. Army. Pp. 330; 4 illustrations. New York: The Macmillan Company, 1923.

THE present volume is one of a series of books that the Macmillan Company are presenting to the medical profession on the more remote and the historical phases of medicine. The medicine man is partially a historical study but largely a sociological study of the character of Shamanism. It is a most complete exposition and one which has the added attraction of being well written and interestingly written, so that the medical man in his spare moments may read with pleasure what his distant connection, the medicine man, does for his savage patients. M.

THE NEW PHYSIOLOGY IN SURGICAL AND GENERAL PRACTICE. By A. RENDLE SHORT, M.D., B.S., B.Sc. (Lond.), F.R.C.S. (Eng.), Member of Council, British Association of Surgeons; Examiner in Physiology for the F.R.C.S., Surgeon, Bristol Royal Infirmary. Fifth edition. Pp. 330. New York: William Wood & Co., 1922.

THE fifth edition of this small book has been considerably enlarged. It has been increased by the addition of three new chapters, one of which, Chapter IV on The Dietetic Factor in the Causation of Appendicitis, might well be omitted. Otherwise the book preserves its very interesting, non-controversial method of presentation throughout and should make most interesting reading for those interested in applied physiology. M.

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THE RIDDLE OF THE RHINE. By VICTOR LEFEBURE, Officer of the Order of the British Empire (Mil.); Chevalier de la Legion d'Honneur; Officer of the Crown of Italy; Fellow of the Chemical Society. Pp. 282; 5 illustrations. New York: E. P. Dutton & Co., 1923.

THIS volume is not truly in any sense a medical publication but it will appeal to the medical man who is interested in war and war chemistry. The book has to do almost entirely with the gases used in attack during war and the problems connected with their use. M.

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A SYNOPSIS OF MEDICINE. By HENRY LETHEBY TIDY, M.A., M.D., B.CH. (Oxon.), F.R.C.P. (Lond.); Assistant Physician to St. Thomas's Hospital; Physician to the Royal Northern Hospital; formerly Assistant Clinical Pathologist and Medical Registrar to the London Hospital. Third edition, revised and enlarged. Pp. 985. New York: William Wood & Co., 1923.

THE popularity of this work is amply attested by the fact that within eighteen months the book has reached its third edition. There is presented in outline form an enormous amount of information, readily available for hasty reference or review, and should therefore recommend itself highly to practitioner, teacher and student. The present new edition has been thoroughly revised; many articles have been rewritten, including those on glandular fever, asthma, hayfever and others; while new articles have been added on a number of subjects. The new material added shows careful and conservative judgment on the part of the author.
K.

# PROGRESS
OF
# MEDICAL SCIENCE

## SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.

ASSOCIATE PROFESSOR OF APPLIED ANATOMY IN THE MEDICAL SCHOOL AND ASSOCIATE PROFESSOR OF SURGERY IN THE SCHOOL FOR GRADUATES IN MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL AND NORTHEASTERN HOSPITALS.

**Cancer of Bladder and Radium Implantation.**—SMITH (*Jour. Urol.*, 1923, **9**, 217) says that the implantation in bladder cancer of bare tubes of radium emanation of low potency or of radium bearing needles of 5 mgm. each, will cause complete necrosis of the tumor, provided, they are inserted 1 cm. apart, and are so placed that the entire periphery of the growth is brought within reach of rays of lethal power. Two classes of cases are suitable for this treatment: Small single papillary carcinomata, into the base of which bare emanation tubes may be deposited by intravesical methods; and sessile carcinomata or the bases of large fungating growths after destruction of the tumor by cautery, into which radium may be implanted through a suprapubic cystotomy. It is inadvisable to bring about the necrosis of a tumor more than 3 or 4 cm. in diameter, as the absorption of toxins from the infected slough is likely to prove fatal. The problem in treating cancer of the bladder by this method is to use enough radium to destroy the cancer, but not enough to destroy the patient. A number of cases of cancer of the bladder, in whom the growth could not have been excised successfully, have shown complete disappearance of the growth clinically, following the implantation of radium.

**Idiopathic Cyst of Common Bile Duct System.**—KIPF (*Arch. f. klin. Chir.*, 1923, **123**, 635) says that idiopathic common duct cyst is a very rare phenomenon, for but 45 cases have been collected—usually discovered in the course of sections. The clinical picture in clearly marked cases gives characteristic but not differentiating symptoms of upper abdominal tumor, intercurrent jaundice, pain and stools without bile. Differential diagnosis must consider or exclude empyema or hydrops or gall-bladder, echinococcus and pancreatic cysts. The

pathological anatomy gives a cystic tumor in close relation to the body walls. The liver is thrust upward by the mass while the ligamentum hepato-duodenale is put greatly upon the stretch. The intrahepatic ducts are distended, the liver itself shows the typical picture of biliary cirrhosis. The histological picture confirms the gross findings: Chronic inflammation with marked round-cell infiltration. The cyst wall usually shares in these degenerative changes.

**Study of Phenol-camphor Action in Joints.**—HEDRT (*Arch. f. klin. Chir.*, 1922, **122**, 19) says the fundamental principles are small incisions, whenever possible, with drainage at the most dependent point; filling of the joint capsule with phenol-camphor; closure of the capsule and movement at the earliest time possible. Experimental researches show that the injection of phenol-camphor solution into the joint cavity does not injure the synovial membrane or the cartilage. The course of healing was quite uncomplicated, and greatly shortened. Cases followed up show very good function and radiographic studies in these cases showed no evidence of arthritis deformans.

**Experimental Intraperitoneal Division of One Ureter.**—JONES (*South. Med. Jour.*, 1923, **16**, 188) says that complete division of the ureter is an exceedingly grave occurrence, but not necessarily fatal. The chief symptoms in the author's animals were anorexia, weakness and diarrhea. Most of the animals were quiet the greater portion of the time. These symptoms are about the same as those found by other observers, except that they observed convulsions and coma rather frequently. The most striking features of our experiments as well as those of other investigators is the activity of the tissues in the vicinity of the severed ureter in preventing the spread of escaping urine. In some instances the reaction is so prompt that the ureteral opening is sealed at once. More frequently a urinary sac is formed by adhesions between the intestines, omentum and body wall. The amount of infection in the peritoneum, retroperitoneal tissue and abdominal wound was surprisingly small.

**The Chronic Appendix.**—MAINGOT (*St. Bartholomew's Hosp. Jour.*, 1923, **30**, 86) says that chronic lesions of the appendix are macroscopic; an appendix that looks normal is not in the least likely to give rise to symptoms and that, therefore, these must be looked for in other organs. The gridiron incision, while it may be useful in certain cases of acute appendicitis should never be employed when dealing with chronic appendicitis, for it is a physical impossibility to explore satisfactorily through McBurney's muscle-splitting incision.

**Gangrene of Penis and Scrotum.**—ESAU (*Arch. f. klin. Chir.*, 1923, **123**, 635) clarifies the etiology of this condition arising from so many possible sources. He groups his causes as follows: (1) The result of constitutional or generalized infections; (2) from urinary extravasation and infiltration; (3) from traumatic agencies, mechanical, chemical and thermal; (4) and most important, localized processes of infection. The whole picture parallels the so-called "phlegmons," which are often noted upon the arms and legs. Although the pathology is

superficial, the disease is very serious. The deeper processes of the gangrene vary—destruction by necrosis encompassing the entire genitalia only in fatal cases. Prognosis is especially guarded, for the subjects are often wasted by disease. The time at which treatment is instituted is important for every hour of delay is exceedingly costly. The author advises and outlines an energetic and radical surgical treatment.

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**Renal Aneurysms.**—VOGELER (*Deutsch. Ztschr. f. Chir.*, 1923, **176**, 312) found that renal aneurysm arose directly from traumatism 18 times, while 11 cases were of spontaneous origin. The trauma was always of considerable violence; as falls from a horse, crushes between cars or against walls, or from knife wounds. The force was always acting directly over the kidney region. Two great factors in diagnosis besides the history are the tumor, and blood in the urine. Twenty-five of the cases were followed completely. The 18 unoperated cases showed after the trauma, bleeding, increasing intermittent hemorrhages, terminating in death. Of the 7 operated, only 1 died.

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**Blood Clotting Through Blood Transfusion.**—STEGEMANN (*Arch. f. klin. Chir.*, 1923, **123**, 759) says that the direct action consists in the introduction of all the elements necessary for blood coagulation. However, but little is known of the hemolytic and coagulating principles. The vaso-constricting principle is of first importance. The indications for this method are, of course, quite limited. It is reserved for hemophilic states and those advanced stages of anemia following hemorrhage, in which heroic measures are necessary. The direct method of transfusion is preferable in these cases.

## THERAPEUTICS

UNDER THE CHARGE OF

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AND

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**Studies On the Bio-assay of Pituitary Extracts.**—SMITH and MCCLOSKY (*Pub. Health Rep.*, 1923, **38**, 493) discuss the unsatisfactory status of the artificial standards for the physiological assay of pituitary extracts. They describe a method for the preparation of a powder of uniform potency, representing the entire ecbolic and pressor activity of the infundibular lobe of the pituitary gland, which does not deteriorate, and from which the active principles are readily extracted. Nine commercial extracts were purchased in

the open market and tested by the usual guinea-pig uterus method against the new infundibular extract. These commercial products varied greatly in activity, the strongest being no less than eight times as powerful as the weakest. One preparation which, according to the claims of the manufacturer, represented 30 gm. of fresh infundibular substance per 100 cc of solvent, assayed at less than 1 per cent. The author recommend that their powder of infundibulum be used as a standard and that manufacturers be required to make and to standardize their extracts to represent the activity of 4 mg. (equal to 30 mg. of fresh gland substance) per 1 cc of finished extract.

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**The Postural Treatment of Diseases of the Bronchi.**—SCHAEFER (*Klin. Wchnschr.*, 1923, **2**, 252) reports surprisingly good results from the Quincke treatment of diseases of the respiratory system whose chief symptom is profuse expectoration. The treatment consists of assuming that position which favors drainage of the diseased lung. When first instituted, the patient is taught to lie flat in bed without pillows and to remain quietly in this position for from thirty minutes to two hours. After two or three days, the foot of the bed is raised 30 cm. and subsequently the head is lowered below the level of the rest of the body and is supported by pillows on a low chair at the side of the bed. The patient lies on his healthy side to promote passive drainage of the diseased area. Splendid results are reported from the treatment in bronchiectasis, lung abscess, fetid bronchitis, and so on. In 1 case, the morning expectoration was decreased in the course of three weeks from the unusually large amount of 500 cc to nothing. If the upper lobe is the seat of the disease, the postural treatment is less successful, since drainage is difficult. No untoward symptoms (hemoptysis, nausea, dizziness, excessive coughing) complicated any of the cases treated by the postural method.

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**The Mechanism of the Vomiting Induced by Antimony and Potassium Tartrate (Tartar Emetic).**—Emesis may occur as the result of direct or reflex excitation of the vomiting center. The reflex may arise from irritation or inflammation of any region of the alimentary tract or of some other organ. It has been shown that tartar emetic acts on the stomach to induce emesis after its oral administration, that only traces occur in the vomitus after its intravenous injection and that it does not cause emesis when applied directly to the vomiting center. WEISS and HATCHER (*Jour. Exper. Med.*, 1923, **37**, 97), working with cats, found that the intravenous injection of tartar emetic caused typical vomiting movements after total extirpation of the entire alimentary canal. Vagotomy, while not always preventing nausea, invariably inhibited vomiting; simultaneous section of the vagi and extirpation of the stellate ganglia prevented both nausea and vomiting after intravenous injection of tartar emetic. Excision of the celiac ganglion and section of the vagi just below the diaphragm did not prevent vomiting. Cutting of the vagi prevents vomiting after the introduction of large but not of massive doses, and vagotomy has less effect on the emetic action of large doses introduced into the lumen of the duodenum than when these same amounts are introduced into the stomach. Atropine has very much the same effect on emesis as vagotomy, but

larger doses are required to suppress emesis when tartar emetic is introduced directly into the stomach than when it is injected intravenously. It seems probable, therefore, that the heart is the site of the origin of the reflex vomiting following intravenous injection of tartar emetic. The drug induces afferent emetic impulses which pass from the heart to the vomiting center by way of the vagus and to a less extent *via* the sympathetic nerves. The introduction of tartar emetic into the stomach arouses afferent emetic impulses which pass upward chiefly *via* the vagus, only a few being transmitted over the sympathetic nerves. The introduction of tartar emetic into the duodenum induces emetic impulses, which pass to the vomiting center over the vagus and sympathetic nerves. The path taken by the afferent emetic impulses induced by tartar emetic in the gastro-intestinal tract seems to depend on the innervation of the organ concerned and not on any selective action of the posion on the afferent nerve.

**The Vitamin Content of Certain Proprietary Preparations.**—COWARD and CLARK (*Brit. Med. Jour.*, 1923, **1**, 13) conclude from the experiments that under normal conditions of life an adequate supply of vitamins can be easily ensured by including in the diet a suitable amount of "protective foods,"—milk, butter, green vegetables and fruit—and that no advantage is gained by trying to obtain the substances in the form of such proprietary preparations as metagen, maltoline, roboline, virol, vitmar and Mellin's food.

## PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.,

OF PHILADELPHIA.

**Suction in the Treatment of Laryngeal Diphtheria.**—LITCHFIELD and HARDMAN (*Jour. Am. Med. Assn.*, 1923, **80**, 524) claim that the pseudomembrane is less intimately attached in the larynx and trachea than it is in the throat. Its removal does not leave as much bleeding. They report a case of laryngeal diphtheria in which their method relieved the obstruction immediately. They feel that suction is especially to be advocated for cases in which there is a low membrane, which cannot be reached by either intubation or tracheotomy. Laryngoscopical examination with suction in severe cases may be repeated when necessary every six or eight hours. It is interesting to note that many of the cases required but one treatment, and in these the membrane was loose in the larynx. In reference to the cases in which suction and intubation were performed, these being only 16 per cent of the total number of cases in which suction was employed, it was noted that intubation was necessary only because of a persisting edema. Convalescence from laryngeal diphtheria has been shortened

by sparing intubation patients, the strain that they were formerly subjected to in the desire to avoid intubation. The avoidance of intubation has no doubt diminished the incidence of chronic cases or patients who cannot endure the removal of the cannula. By employing visually guided suction the mortality was reduced. To perform suction the patient is wrapped in a mummy bandage as for intubation, and through a Jackson laryngoscope the membrane and mucous are aspirated by means of a No. 16 to 18, French silk or metal catheter, which is connected to an aspirating bottle, and in turn to an ordinary electric suction pump.

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**Bacteriology of the Urine in Acute Nephritis in Children.**—HILL, HUNT and BROWN (*Am. Jour. Dis. Child.*, 1923, **25**, 198) studied 21 cases. They found the urine sterile in 16. In 2 cases, Staphylococcus albus was found. This was probably a contamination. A diphtheroid organism was found in 1 case and colon bacillus in 2 cases. The cases which showed the latter had high leukocyte counts with a good deal of pus in the urine, as well as blood and casts, due probably to a complicating pyelitis. Only 2 patients showed fever during the course of the disease, although it is possible and probable that in many cases fever was present at the onset before the child entered the hospital. One of these patients had cervical adenitis, which accounted for the fever, and 1 had a complicating pyelitis. The leukocyte count was elevated above 16,000 in 6 cases. In two of these, it was accounted for by the presence of a complicating pyelitis. In 3 cases, it was accounted for by the presence of a cervical adenitis. These results indicate that in most cases of acute nephritis in children, after the disease has once been established, there are no bacteria demonstrable in the urine and there are probable none in the kidneys. There is no fever and no elevation of the leukocyte count. These results do not rule out the possibility of bacterial infection at the very onset of the disease, and this is very strongly probable. According to some workers, bacteria are taken up by the polymorphonuclear and endothelial cells in the glomeruli, and in a very short time toxins are liberated by the rapid lysis of bacteria within the glomerulus. This causes the injury that is produced. This hypothesis is borne out by clinical observation on children suffering with acute nephritis. It is also possible that it is not the bacteria but soluble toxins absorbed from the infected focus, such as tonsils, cervical glands and the like produce the injury to the glomeruli.

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**Types of Organisms Found in a Series of Tuberculous Children**—GORDON and BROWN (*Am. Jour. Dis. Child.*, 1923, **25**, 234) in a total of 30 cases of tuberculosis in children under the age of twelve years, noted the bovine organism in 10, or 33.3 per cent. Of the total number of patients twenty-three were less than five years of age. In six of these the organism was the bovine. This represented a percentage of 25. The remaining 7 patients were between the ages of five and sixteen years, and of these there were 4 instances of bovine infection, or 52 per cent. From these figures, it can be seen there was a greater actual incidence of bovine infection in the children under five years of age, although the number of bovine cases in patients between the ages of five and

twelve was relatively greater. In the infants under one year of age, the bovine organism was identified only once. Of the total number of the cases, 22 were known to have been fatal. Of this number four, or less than 20 per cent, were of the bovine type. Autopsy was performed in 12 of the fatal cases. Of this group the cases, in which the point of origin of the infection was found in the alimentary tract, proved to be all bovine. The human bacillus was recovered from all of those cases in which the point of origin at necropsy was in the respiratory tract. In 5 cases out of the total number, the history indicated that the children were exclusively breast-fed. Four of these showed a human type of infection and 1 the bovine, and this probably had received cow's milk after having been weaned from the breast. Seven cases of the total number gave a definite history of either familial tuberculosis or contact with tuberculous persons. Of these, 6 cases proved to be infected with the human type of organism and one with the bovine type.

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**Internal Hemorrhagic Pachymeningitis in Infancy.**—BURHANS and GERSTENBERGER (*Jour. Am. Med. Assn.*, 1923, **80**, 604) report 5 cases of internal hemorrhagic pachymeningitis, which were observed in their clinic within a period of three years. This corroborates the opinion of Finkelstein and Rosenberg, that the condition is more common in infancy than is generally believed. From the standpoint of etiology, in this series of cases, infections, especially diphtheria and syphilis, can be excluded in every instance but one, in which syphilis may be considered by some to have been a possible factor. From the standpoint of etiology, a poor state of nutrition can be positively excluded in 3 of these 5 cases, as 2 were exceptionally well-developed and nourished infants, and the third was also in a very good state of nutrition. The other 2 patients were in a very bad state of nutrition, but this was just as possibly a result as a cause of the pachymeningitis. Trauma can be implicated as a factor in 4 of the 5 cases. It would seem that subacute pachymeningitis from birth hemorrhage, rendered acute by further physical injury, would explain the development in some of these cases. In certain groups of infants there may be a definite predisposition toward the development of pachymeningitis. The prominent symptoms in these cases were retinal hemorrhage in 4 cases. In the one in which this was absent there was the largest collection of fluid in the subdural space. A positive fontanel puncture was obtained in 3 cases in which it was performed. In 1 case, a characteristic fluid was obtained by spinal puncture. In the fifth case puncture was not done because of parental objections. As the latter 2 children were about one year of age, and retinal hemorrhage was present, it is probable that a fontanel puncture would have given positive results. Convulsions were present in every case, but as convulsions occur as a result of other injuries and conditions their appearance is suggestive, but not pathognomonic. Bulging of the fontanels was absent throughout the period of observation in 3 cases, and in a fourth the fontanel did not bulge until the second admission, when it bulged slightly. In the fifth case there was slight bulging on admission. The absence of bulging of the fontanel does not speak against internal hemorrhagic pachymeningitis. A general state of collapse or widening

of the sutures may be sufficient to counteract the incroachment on the intracranial space by the development of a pachymeningitic cyst. Enlargement of the head was not definitely present in any of these cases. In only 1 case was there a possible enlargement. Nasal discharge was present in 3 cases and in 2 of these it was bloody in character. In 1 of these patients, the discharge did not develop the bloody character until long after marked evidence of the pachymeningitis had been observed. As no evidence of syphilis or diphtheria was found in any of this series, it may be concluded that the nasal discharge was a coincidence or a result of the pachymeningitis, and not a symptom of an infection responsible for the development of the disease. In two of the cases in which the calcium content of the fluid obtained through the fontanel puncture was determined, it was found to be decidedly lower than that of the blood serum, whereas the inorganic phosphorus content of the fluid and the blood serum was practically the same. Since these figures are the same as the results usually obtained by determinations on whole blood it would seem logical that the fluid in these subdural cysts is blood, unaltered except for the solution or digestion of all or a part of the red corpuscles. This is not supported by the amounts of sodium and potassium, which were the same as in the serum, nor by the percentage of protein, which showed a wide variation. The coagulation time and the bleeding time were normal in the 3 cases in which the tests were performed.

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**Calcium Absorption in Children in a Diet Low in Fat.**—Holt and Fales (*Am. Jour. Dis. Child.*, 1923, **25**, 247) found that a marked reduction of fat in the diet of children changed the character of their stools from smooth, normal, alkaline, and well digested to acid, foul, with an excess of fermentation and undigested food residues. Whether this change was due to reduction of the fat or the increase of carbohydrate or to both factors is impossible to say. In 5 of the 7 cases, the calcium absorption was markedly reduced when the low-fat diet was taken, and in 3 cases, a negative balance was produced. In the other 2 cases, the stools were never entirely normal, even during the control period, and the absorption was not lower on the low-fat diet than it was on the control diet. These two children were very much alike so far as digestion and general symptoms were concerned. The chemical findings in these two cases were almost identical. It is impossible to offer any explanation of the difference of the results in these two cases and those obtained in the other five. The increase of calcium oxide excretion was in most instances due partly to the fact that on the low-fat diet the daily amount of total solids in the stools was markedly increased, and partly to the fact the calcium oxide percentage of total solids of the stool was higher. In all but 1 case, the total solids of the stool were increased on a low-fat diet. In 4 cases the calcium percentage of solids were increased. In all cases but one, the total ash percentage in the stool was higher on the low-fat diet. Although the results of these investigations were not altogether uniform, the indications are that a low-fat diet greatly diminishes calcium oxide absorption. Whether the calcium absorption is dependent on a definite relation between fat and calcium in the diet, or whether the fat intake influences the calcium oxide absorption chiefly by the maintenance of

proper digestive conditions, it is impossible to say. It is quite certain that a very low-fat intake brings about abnormal digestive conditions as judged by the type of stool. The conditions for proper calcium absorption are much better when the fat intake is generous.

**A Comparative Chemical and Clinical Study of Boiled Butter and Cream in Infant-feeding.**—LOWENBURG (*New York Med. Jour.*, 1923, **117**, 295) claims that volatile fatty acids exist in butter in even less stable combinations than in cream. By boiling butter slowly for five minutes, over 50 per cent of these acids are driven off. Boiling butter for two minutes is sufficient for clinical purposes, but from three to four minutes is a safer average. Sweet butter contains less volatile acids than does the salted. Boiling cream does not materially change its acid content. Boiled butter may be added advantageously in varying and gradually increasing quantities to skimmed milk formulas and to other food combinations. Boiled butter appears to be a more acceptable addition to milk formulas than does cream. The presence of flour or other forms of starch though acceptable to insure an even distribution of fat are not necessary essentials to the digestibility of boiled butter. Vomiting and diarrhea are neither inaugurated nor made worse by the addition of boiled butter, but may often cease. Constipation has been the rule, and the reaction of the stool has been found to have been feebly or markedly alkaline. All cases free of parenteral disturbances, to which this substance has been fed, have experienced a uniform gain in weight of from 1 to 2 ounces a day.

## OBSTETRICS

UNDER THE CHARGE OF

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**Delivery of the Arms and Head in Labor with Breech Presentation.**—Before a recent meeting of the Münchener Gynecological Society (*Monatsschr. f. Geburtsh. u. Gynäk.*, 1922, **59**, 101) occurred an interesting discussion on this subject. Attention was called to the necessity of avoiding strong and forcible traction upon the body of the child in these cases. Smellie's advice to apply forceps to the after-coming head had been followed by the majority of obstetricians for a considerable time. Schroeder had opposed this, and this use of the forceps had been largely abandoned. In more than 40 cases in the Münchener Clinic since 1912, the forceps had been applied to the after-coming head with very good results. In discussion, the point was brought out that the successful use of forceps called for patience, skill and the avoidance of considerable force. The instrument must also be accurately applied to the sides of the child's head. In Continental clinics the Näegeli forceps is often applied in the transverse

diameter of the pelvis. Attention was also called to the danger of cerebral hemorrhage in the infant, following laceration of the tentorium in breech extraction. In 291 cases reported in the literature, this accident occurred in 37 per cent of those children delivered by extraction. This is the result of pressure, much of which comes as the head passes through the partly dilated cervix. The best results are obtained by the use of forceps to the after-coming head and Kieland's comparatively new instrument is especially good for this purpose. It may be necessary to incise the cervix before extracting the head. Döderlein had obtained excellent results from the use of forceps to the after-coming head and was strongly in favor of its employment.

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**Treatment of Placenta Previa by the use of the Dilating Bag.**—ZIMMERMANN (*Monatsschr. f. Geburtsh. u. Gynäk.*, 1922, **59**, 94) presented a paper upon this subject, which was discussed at considerable length in the Münchener Gynecological Society's meeting. The criticism was made that while in the hands of an expert the use of the dilating bag in placenta previa gave excellent results, when employed by those not skilled and expert, the introduction of such a bag might separate the placenta and increase the bleeding. While this hemorrhage might not be severe and the blood pass between the placenta and the bag, it would still form an important element in turning the tide against the patient. Others preferred the extra-ovular use of the bag in these cases. This is thought to be the simpler method and productive of quite as good results as combined version and introduction of the bag through the placenta within the fetal sack. This method has a further advantage in that it can be applied by a physician without assistance in the home of a patient in cases where circumstances make it impossible to take the patient to a hospital or to summon further assistance. Others call attention to the danger of treating cases by the use of the tampon and combined version. One case was reported where in a multipara a firm tampon was applied and twenty-four hours later version was performed. This was followed by the death of the patient an hour afterward from hemorrhage caused by relaxation of the uterus. It was also thought exceedingly dangerous to proceed at once with the extraction of the child after combined version had been performed. Where patients enter hospital in good condition, not infected or greatly weakened by hemorrhage, it is possible to secure fairly good results. In the clinic in Bonn, Germany, in 72 cases the mortality among the mothers was 2.8 per cent, with a fetal mortality of 57.7 per cent. These results were obtained by the use of the dilating bag. Where combined version was employed, fetal mortality rose to 66.7 per cent. In another clinic, vaginal section had been employed successfully. In a series of 104 cases reported from one clinic, one-third of them were between seven and eight months in pregnancy. In 19 of these the treatment employed consisted of rupturing the membranes; in 15 Cesarean section was done successfully for mother and child, with the exception of one mother having contracted pelvis, who died of grippe-pneumonia. There was a strong statement from one operator to the effect that he had never seen an efficient and properly applied vaginal tampon in these cases. He considered such application as useless and very apt to be followed by the development

of infection. Streit described the case of a multipara, aged forty-one years who had a contracted pelvis. This patient had previously had difficult labors. At the end of the sixth month she had a hemorrhage and remained in bed when the hemorrhage ceased. She was able after this to go about and entered hospital for the induction of labor. Hemorrhage occurred soon after. It was found that the child was in transverse position and that there was partial placenta previa. The membranes had not ruptured and a loop of the umbilical cord had prolapsed in the membranes. The bleeding from the lower uterine segment was excessive but was controlled by the tampon. Five hours later, after the introduction of the dilating bag, the case was terminated by version and extraction, with good results for mother and child. Attention was drawn to the comparative merits of dilating bags made of rubber and those made of animal membrane. It was also thought of the greatest possible importance that midwives be instructed to immediately send all patients to hospital who developed hemorrhages during pregnancy, and in such cases to abstain entirely from internal examinations.

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**Ectopic Gestation in the Ninth Month.**—TSCHAMER (*Monatsschr. f. Geburtsh. u. Gynäk.*, 1922, **59**, 136) described the case of a woman, aged thirty-five years, who sixteen years previously had born a child in spontaneous labor. The patient had believed herself pregnant, but the abdomen grew less instead of greater in size. She had no pain or disability, and the movements of the child ceased, and the breasts no longer increased in size. A midwife made a diagnosis of the death of the fetus and prophesied its speedy expulsion. Five weeks passed without labor, and the patient went to the hospital, where she was given quinine, ergot and pituitrin, with the result of causing some dilataton of the cervix, but practically nothing else. Some time after, the abdomen decreased suddenly and considerably in size, and apparently fluid and solid material seemed to have been passed. The patient then become considerably weakened and depressed in general health and sought advice at the clinic. On examination, the patient was of moderate stature, anemic and weak, with fine rales and rough breathing over the lungs. Over the apex of the right lung there was dulness. The abdomen showed a central tumor arising from the pelvis and reaching above the umbilicus, whose exact nature could not be made out. No heart sounds or movements could be elicited. On vaginal examination, the cervix was hard and firm and apparently a difference could be made out between the uterus and the abdominal tumor. The rectal examination was negative. It was thought that the abdominal tumor might be a tuberculous mass or an ovarian cyst or pregnancy. On operation, the peritoneum was thickened and adhered to the wall of the tumor. On opening this there was a cavity filled with offensive reddish brown fluid and whitish masses. In this was the skeleton of a child at full term. The soft parts of the child had entirely disappeared, leaving the complete skeleton. The sack was emptied and cleansed, packed with iodoform gauze, and drained. A fistula with the bowel developed, which gradually closed, and the patient made a good recovery. On putting the pieces of the skeleton together, and measuring, it was found that the

child must have been about 45 cm. long, which corresponded with the patient's history. A similar case was reported in 1899 to the Obstetrical Society of Vienna by Knauer. In this case although the abdomen was opened, the fetal sack was taken for a malignant ovarian tumor, and nothing more was done, the abdomen being closed. Seventeen days later, the lower end of the abdominal incision opened and a portion of the fetal skeleton protruded, and ultimately the entire skeleton of the fetus at eight months was expelled.

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**Labor Complicated by Rupture Into the Rectum of a Dermoid Ovarian Tumor.** — DAVIDSON (*Jour. Obst. and Gynec. Brit. Emp.*, 1922, **29**, 376) describes the case of a multipara with delayed labor in whom the attempt was made to deliver by forceps. While traction was being exerted, a tumor, shaped like a sausage, bulged through the anus and on being pushed aside burst, extruding sebaceous material and hair typical of dermoid tumor. The child was delivered, the base of the tumor ligated and the mass was cut away. On examining through the rectum the ligature could be felt extending up to a tear in the bowel and leading into the peritoneal cavity. The abdomen was at once opened and the remainder of the tumor removed. Supra-vaginal hysterectomy was performed, and the perforation in the bowel was closed and drainage inserted through the posterior fornix. The patient's recovery was complicated by bronchitis, infection of the tonsils and pyelitis; later by bronchopneumonia. Two months after the delivery the patient was well with the pelvis clear. There was no discharge of fecal matter through the wound, and apparently the tear in the intestine closed completely. Colostomy might have been performed in place of suturing the bowel.

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**Interstitial Pregnancy After the Removal of Tube and Ovary on the Same Side.**—MCINTYRE (*Jour. Obst. and Gynec. Brit. Emp.*, 1922, **29**, No. 2) reports the case of a patient who for four and a half years had periodic attacks of sharp and cutting pain in the left iliac fossa and lumbar region. Abdominal section was performed, and the right tube and ovary were removed. Three years later she entered hospital with the history that eighteen months after her first operation she gave birth to a child in normal labor, the pregnancy having been normal and the child being nursed normally for some time. Menstruation returned six weeks after the birth of the child. There had been disturbance in menstruation, and the patient had felt ill for two weeks. two days before admission, she fainted and later had severe pain in the abdomen. This disappeared on rest, followed by severe pain in the small of the back and vomiting. On admission to hospital the patient was collapsed; the abdomen soft but tender; the tenderness most marked in the left iliac fossa. There was dulness in both flanks, and a boggy fulness behind the uterus. On section there was a large quantity of blood in the abdomen, and on the right side of the uterine wall, where should have been the stump of the right Fallopian tube, there was a ragged cavity, containing blood clot. This was resected and the uterine wall sutured. The patient's recovery followed. On examining the specimen, chorionic villi were found, and no trace of the stump of the Fallopian tube. Microscopical examination showed

no trace of tissue belonging to the tube. The impregnated ovum had been in the uterine wall. At the first operation the stump of the tube was ligated and evidently the lumen of the tube must have been reëstablished. As the ovary on the right side was removed, the ovum must have been discharged from the left ovary.

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**Cullen's Sign in Ectopic Pregnancy.**—F. H. JACKSON (*Jour. Am. Med. Assn.*, 1922, **79**, 1929) had made an interesting observation concerning Cullen's sign in ectopic pregnancy. He had occasion to examine a very obese young woman whose history indicated ectopic gestation. The abdomen was decidedly heavy, but the dark bluish discoloration at the umbilicus described by Cullen could not be made out. The patient was examined then in a dark room with a light directly on the umbilicus. The room was dark and one of the modern flash lights was focussed on the umbilicus. The greenish blue discoloration could then be made out. A vaginal examination in the case was suggestive but not definite. The patient was removed to hospital and operation disclosed an unruptured gravid tube, a large amount of free blood in the abdominal cavity and an ovarian cyst on the side corresponding to the gravid tube. The cyst was the size of an orange and was attached to the sigmoid and posterior broad ligament, with the gravid tube situated on top.

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**Unsuspected Pregnancy.**—MURRAY (*Lancet*, 1922, **2**, 1073) reports the case of a woman aged twenty-four years, who twenty-nine hours before she was seen had been delivered of a 6½ pound child apparently at term. She had been married for three years, and during that time had passed through a severe attack of typhoid fever and had lost much weight. On her recovery she began to gain. Menstruation had always been scanty and infrequent, and following the typhoid there was for some time complete cessation. There was, however, a distinct history of some menstrual discharge each month during the nine months of pregnancy, and for this reason she supposed that this was the natural period. There had been no vomiting and the patient had felt no movements, had had no idea that she was pregnant, although the abdomen became large between the seventh and eighth months. After an attack of supposed indigestion there was pain in the abdomen. This increased in severity and the birth of the child occurred unaided followed by the normal delivery of the placenta. There were several lesions in the vagina which produced continuous oozing. These were closed under anesthesia and healed promptly. In the mother's efforts to extract the child the fingers had been introduced into the child's mouth and its palate was scratched in several places. So positive had the patient been concerning the occurrence of normal menstruation that she had made no preparations whatever for the birth of a child.

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**Lumbar Puncture in the Treatment of Eclampsia.**—SPILLMAN has revised the literature of this subject to determine whether in eclampsia this method of treatment is justifiable (*Am. Jour. Obst. and Gynec.*, 1922, **4**, 568). The normal pressure in the spinal canal is 120 mm. of water. In eclampsia the pressure is found to range from 120 to 600. As to whether this treatment is dangerous in eclampsia it is

impossible to positively assert. Lumbar puncture is sometimes followed by cerebral complications which may be serious. Where infection of the blood-stream is present lumbar puncture predisposes to meningeal infection. As to the influence of lumbar puncture on the recovery of the patient, in 68 reported cases the mortality was 27.6 per cent. In 25 of the 68 cases convulsions ceased after the puncture, but in 2 of these cases the puncture obtained no fluid from the spinal canal. Among these 25 patients, 4 died; 3 of the deaths were due to streptococcus infection; 1 to pneumonia and 1 to hemorrhage into the brain.

It is usual to withdraw from 20 to 30 cc of fluid, but as much as 101 cc of fluid have been withdrawn at one time with recovery. The finding of blood in the spinal fluid does not mean that there has been fatal intracranial hemorrhage, although it is an indication of a serious condition.

## GYNECOLOGY

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**Radiotherapy of Myopathic Bleeding.**—In reporting the final results of radiation in a series of 183 cases of myoma and myopathic bleeding, MILLER (*Surg., Gynec. and Obst.*, 1922, **34**, 593) believes that he can prove that radiation will eventually supplant surgery in a large percentage of cases now treated by hysterectomy. Since it may be inferred that the writer is overenthusiastic in regard to the use of radium, he states that during the same period of time covering this series he has operated upon an equal number of cases, so that it can be shown that he appreciates the limitations of radium, and is by no means insistent that it can supplant surgery in all cases of myoma or essential hemorrhage. The age of the patient, the type and social situation, as well as the size of the tumor, the condition of the appendages, the evidence of previous infection and the general condition of the patient are all factors to be carefully weighed in determining the most satisfactory method of treatment. The most striking feature revealed in a review of both series of cases, those treated by radium and those treated by surgical intervention, is the increasing percentage of myomectomies performed where formerly hysterectomy would have been done. The prevalent idea that myomectomy is attended with a high mortality and that second operations are necessary in too large a percentage of cases to warrant conservatism is not borne out by the results obtained by competent surgeons. The decision to

resort to myomectomy in many cases which would have been subjects for hysterectomy formerly was prompted by the assurance that if myomectomy failed to control the hemorrhage or check the menstrual disorders radium would complete the cure without further surgical interference. With such assurance, the scope of conservative surgery has been materially widened, a larger number permanently relieved and the percentage of subsequent pregnancies has further justified the decision. The average time of exposure in young women in this series, that is, women under thirty-eight years of age, was twelve hours in cases of myomata. In women beyond this age, where it was not so important to preserve menstruation, the treatment lasted twenty-four hours. As a rule, 50 mg. of radium element was employed. This dosage produced permanent cessation of menstruation in women over forty years of age in 94 per cent of the cases. In the writer's earlier work, a second exposure was made within ten days or two weeks, but it was soon observed that this was unnecessary, and often caused discomfort that was persistent, and occasionally very distressing. In this series, 102 reported complete relief of the 107 cases of myoma, from hemorrhage within five months after radiation, while 2 other patients were relieved by a second application. In myopathic hemorrhage in women over forty years, a full radium dose (50 mg. for twenty-four hours) caused immediate cessation of menstruation in 20 per cent of the cases; 60 per cent menstruated once, 15 per cent menstruated irregularly, and the balance reported no relief and returned for a second treatment which was successful in all but 3 instances, 2 of which were relieved by a third exposure. Subsequent reports as to the menopausal symptoms are interesting. In women over forty years, in whom preservation of function was not considered important, about 60 per cent reported flushes and the usual phenomena of the climacterium. In about 20 per cent the symptoms were reported as severe, and almost invariably these cases had given a history of bleeding of the aggravated type. Profuse leukorrhea was noted in about 20 per cent of the cases, and a slight but persistent discharge was reported in 30 per cent, while in about 40 per cent it was absent, or was so slight as to cause no comment. Not infrequently, radium cured or markedly diminished a leukorrhea which was present before its application. The leukorrhea rarely lasted longer than six or eight weeks, although in several instances it was persistent after a year.

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**Vaginal Operation for Prolapsus.**—It is gratifying to CULLEN (*Am. Jour. Obst. and Gynec.*, 1922, **4**, 544) to note that vaginal hysterectomy is gradually disappearing as a means of treating uterine prolapse and, in offering the method which has given him the most satisfactory results, he makes no claim of originality, but admits that he has combined measures from several different operations, especially those of Watkins and Coffe. The operation presented by the writer begins by drawing down the cervix and then making an incision all the way round the vagina fairly high from the cervix, after which a perpendicular incision is begun just below the urethral orifice and continued downward to the circular incision. The mucosa of the anterior vaginal wall is then dissected down from the transverse incision nearly to the external os and the triangular flaps above the transverse incision are dissected

away. The bladder, which prolapses into the wound, is then pushed up and separated from the upper part of the cervix and lower part of the body of the uterus. After the vesico-uterine peritoneal reflection is exposed, it is opened and instead of grasping the uterus with a tenaculum or other forceps, a figure-of-eight suture of chromic catgut is placed in the anterior wall of the uterus, going rather deeply in the wall but taking care not to enter the uterine cavity. This suture is now tied and used as a tractor. This exposes more of the fundus and a second figure-of-eight suture is placed and tied. After three such sutures are in place, the end of each is rethreaded, passed through the peritoneum where it was opened, and then through the edge of the vaginal mucosa. After these sutures have been placed they are clamped, and a small gauze pack is temporarily placed between the bladder and fundus in order that no blood may escape from the vagina into the peritoneal cavity. Strong traction is now made on the uterus from below and the cervix is cut half way through transversely. The cervical canal is then well dilated and the cervix is then completely severed, removing the adjacent posterior vaginal wall with it, as outlined by the primary transverse incision. Douglas's cul-de-sac is occasionally accidentally opened while the mucosa of the posterior vaginal wall is being dissected free, but when this happens it is of little consequence if the rent is immediately sutured with catgut. The vaginal edges remaining are now united to the cervix by interrupted sutures and then the original fixation sutures in the uterus are tied, bringing together the anterior wall of the vagina. The perineum is then repaired and a most satisfactory result will follow according to the writer.

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**Myomectomy.**—In recent discussions on the treatment of uterine fibroids, the alternatives of hysterectomy on the one hand and roentgen-ray and radium treatment on the other have generally been dealt with as though they exhausted the possibilities of treatment. Myomectomy has been almost entirely overlooked. GILES (*Lancet*, 1923, **204**, 178), who is surgeon to the Chelsea Hospital for Women in London, holds the view that in the majority of cases of fibroids requiring surgical treatment, hysterectomy is the more suitable and also the more satisfactory operation, and the scope of myomectomy is restricted to the minority of cases. Hysterectomy requires no justification; it is generally accepted as a sound procedure, surgically and clinically. But myomectomy needs to be justified by its results, and reasons must be stated as to why it should be preferred; its limitations must also be acknowledged and the conditions of its suitability defined. The outstanding claims for myomectomy are: (1) That the uterus is preserved for the important function of child-bearing; and (2) that the patient is thereby spared the mental distress of feeling that an essential part of her womanhood has gone. The broad-minded advocate of myomectomy will at once concede that in a woman who is past the child-bearing age, the first claim disappears and the second has only an academic existence, although there may be reasons for preserving the uterus that are not founded on its child-bearing function. But we may properly narrow the issue to the consideration of myomectomy *versus* hysterectomy in the child-bearing period. We may glance

first at the immediate results, namely, the mortality as compared with hysterectomy; for this purpose the writer believes that his own statistics will serve as well as any. The figures (to the end of December, 1922) are as follows: Hysterectomy for fibroids, 1004 cases, 17 deaths, mortality 1.69 per cent; myomectomy, 173 cases, 3 deaths, mortality 1.7 per cent. There is thus very little difference in the mortality of the two operations, certainly not enough to make this a deciding factor in the choice of operation. What is the likelihood of a recurrence of fibroids? In the present series of 49 cases examined or reported upon by their doctors, the uterus was normal in size without fibroids in 41 cases; it was enlarged without fibroids in 3 cases; in all 44 cases without fibroids, or 90 per cent. In regard to the effect on the menstrual losses, in the present series he excludes 6 cases where the menopause preceded or synchronized with the operation. Of the remaining 47 cases, menstruation was normal and moderate in 36, or 75.1 per cent; and in 11 cases it was profuse, either at first or later on, or there was intermenstrual loss. Taking all the cases together, we find that of 83 cases menstruation was normal in 67, or 80.7 per cent. The conclusion is that there is liability to menorrhagia or metrorrhagia after myomectomy in about 20 per cent of cases. This result is not altogether surprising because it is clear that unless we open the uterine cavity every time we do a myomectomy, some small intra-uterine growth may easily be overlooked. In regard to the serviceability of the uterus for childbearing after myomectomy, this report shows that of 50 women who had the chance of conceiving after operation, 14 became pregnant, or 28 per cent. The author, therefore, claims that judged by the criterion of results, the advantages of myomectomy definitely outweigh the disadvantages in the surgical treatment of uterine fibroids in a restricted class of cases. His own feeling is sufficiently expressed in the fact that of 1177 cases of uterine fibroids treated surgically, hysterectomy was done in 1004, or 85.3 per cent. This proportion of myomectomy to hysterectomy was thus 1 to 6, showing that he applies myomectomy only in a restricted class of cases. Fibroids associated with pregnancy do not necessarily call for surgical treatment. When they are causing no symptoms, and do not seem likely to interfere with labor, it is best to leave them alone, always provided that the patient can be kept under observation so that operation can be undertaken if urgent symptoms arise, and that the medical attendant is on the lookout during labor. Myomectomy during pregnancy is indicated in three groups of conditions: (1) When the tumor or tumors appear to be increasing rapidly in size; (2) when the patient is suffering from pain, pressure symptoms, or indications of septic or degenerative changes in the tumor; (3) when the position of the fibroids makes it probable that labor will be obstructed, in which case myomectomy is done for the purpose of avoiding the necessity for Cesarean section and of allowing the confinement to take place naturally.

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**Treatment of Chronic Leukorrhea.**—A dozen years ago, dilatation and curettage was probably the most frequently performed gynecological operation. This held true for the most prominent clinics as well as for less well known operating rooms. Not only was this a usual operation, but the reason assigned for scraping the uterus was most often

a chronic infection, variously designated as chronic metritis, endometritis or leukorrhea. Observance of the futility of this procedure, particularly its limited value in attempts to relieve discharges, stimulated in CURTIS (*Jour. Am. Med. Assn.*, 1923, **80**, 161) a desire to learn something about chronic leukorrhea and chronic infections of the uterus. These efforts in turn eventually led to a study of diseased Fallopian tubes. He found that a small percentage of chronic leukorrhea cases are due to diffuse pelvic infection, to congested displaced organs and to other kindred lesions, but the overwhelming majority belong to the infected cervix—Skene's duct group. During the last four years he has treated the most severe and persistent cases of chronic leukorrhea as follows: The vicinity of the urethra is searched for infected Skene's ducts and urethral glands. Diseased foci are threaded on the blunt end of a needle, the tract is laid open with a knife, and the lining is fulgurated or otherwise cauterized. The cervix is thoroughly dilated, and radium is introduced into the cervical canal for the purpose of producing atrophy of the infected hyperplastic glands. Recovery has resulted in 90 out of 104 cases treated according to this plan. Whether the endocervix is treated with radium or thoroughly excised according to the method of Sturmdorf is perhaps immaterial. We must remember, however, that the glands in the region of the urethra also demand examination and appropriate attention. The work of the writer in the field of uterine infections has been one of the outstanding contributions of the past decade and his conclusions and recommendations should be carefully considered by all interested in this line of work.

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**Pyelography.**—A rather extensive experimental as well as practical study of the various chemicals used in pyelography has been made by LOWSLEY and MULLER (*Jour. Urol.*, 1923, **9**, 1), as a result of which they have come to rather definite conclusions as to the proper technic as well as proper solution which should be used in this helpful diagnostic procedure. The technic which they recommend is to cystoscope the patient as usual, catheterizing the ureters with lead catheters. Specimens are collected from each ureter and sent to the laboratory for bacteriological, chemical and microscopical examination. A phenolsulphonephthalein test is then performed to determine the efficiency of each kidney before the pyelogram is made. Two roentgenograms are taken before the injection of the opaque material, one of the kidneys and upper ureters and another of the bladder and lower ureters. Sodium iodide, 20 per cent is then carefully injected with a special syringe and as soon as the patient complains of a feeling of fulness some of the solution is allowed to run out and then another roentgenogram is made of the upper tract and one of the lower tract as was done before the injection. A fifth roentgenogram is made with the patient in the erect posture, the catheters having been withdrawn to the ureteral orifices and sodium iodide injected during this withdrawal. They have found that many strictures and other ureteral defects are brought out in this way which are not discernible in the prone position and with the ureteral catheters in place. The sodium iodide is usually drained off by reinserting the catheters, thus relieving instantly the pressure exerted by the injection. It was formerly their

practice to do a pyelogram on only one kidney at a time, but since they have been using sodium iodide they unhesitatingly do bilateral pyelograms. They have found that 20 per cent sodium iodide solution is more satisfactory as a pyelographic medium than any other solutions as it casts a deeper shadow, is non-toxic, non-irritating and is easily prepared. They believe however, that pyelography should be done only in selected cases. Persons suffering from acute or subacute infections of the kidneys, those who are emaciated or in a weakened condition should not be subjected to this examination.

## PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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**The Intestinal Flora in Mouse Typhoid Infection.**—Inasmuch as some mice, in the course of epizootics or after artificial feeding of a strain of *B. pestis caviæ*, do not develop mouse typhoid, it is evident that the mere presence of the organism is not the sole factor, in every case, in producing the infection. In order to determine the other necessary factors, WEBSTER (*Jour. Exper. Med.*, 1923, **37**, 21) determined the normal intestinal flora of 58 mice, receiving a regular diet of bread and milk, by culturing the stools of 50, and the contents from duodenum, ileum, cecum, colon and sigmoid of 8. In addition, 33 mice were divided into groups of 16 and 17, respectively. One group was fed bread and milk for five days, the other raw beef muscle and water for the same period of time. After determining the flora, the animals were given, by stomach tube, 0.5 cc of an eighteen-hour broth culture of *B. pestis caviæ* diluted 1 : 100. It was found that in those mice fed on bread and milk, *B. acidophilus* and *B. bifidus* dominated the floræ about 25 to 1, whereas, when the diet was changed to meat and water, the floræ changed rapidly, the Gram-negative bacilli and certain putrefactive organisms outnumbering all others. This flora did not change after the instillation of *B. pestis caviæ* into the stomach and was the same in those mice which resisted the infection as in those which had succumbed. Furthermore, the mice receiving meat and water and showing a colon, *B. diffluens and B. welchii* flora were equally susceptible to mouse typhoid, as were the mice fed on bread and milk and showing the acidophilus flora.

**Microbic Virulence and Host Susceptibility in Mouse Typhoid Infection.**—From previous observations on an experimental epizootic

of mouse typhoid by a member of the paratyphoid-enteritidis group, *B. pestis caviæ*, it was learned that regardless of the number of bacteria ingested, some mice proved refractory to infection by the gastro-intestinal route, the normal portal of entry. Continuing his work along these lines, WEBSTER (*Jour. Exper. Med.*, 1923, **37**, 231) conducted seven experiments, utilizing over 300 white mice from the stock breeding rooms of the Rockefeller Institute, 26 from Pennsylvania and 28 from New Jersey. All mice were of uniform age and weight, received a diet of bread and milk and were placed in separate sterilized jars. Control stool cultures and blood-agglutination tests were made. All animals were injected *per os* by stomach tube with fixed doses of *B. pestis caviæ*. At short intervals thereafter the stools and blood were examined for the ingested bacteria, the general character of the fecal flora was ascertained and the blood tested for homologous agglutinins. It was found that the mice, under these conditions of experimentation, varied in their susceptibility to mouse typhoid infection. In any series 20 to 30 per cent showed no sign of infection; 5 to 10 per cent presented symptoms of the disease, yielding positive blood cultures and recovered with or without homologous agglutinins; 70 to 80 per cent developed positive blood cultures, and succumbed in a more or less constant ratio relative to time. While the New Jersey mice followed a curve quite similar to that of the 520 standard controls, the Pennsylvania mice were more resistant to infection. The strain of *B. pestis caviæ* employed over a ten-month period of experimentation showed no permanent change in virulence.

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**Contribution to the Manner of Spread of Mouse Typhoid Infection.**—Having called attention to the fact that the spread of mouse typhoid in a given mouse population is determined by three factors, namely, the special and quantitative distribution of the bacilli, the virulence of the microörganism and the susceptibility of the host, and having described experiments dealing with the last two variables, WEBSTER (*Jour. Exper. Med.*, 1923, **37**, 269) conducted contact experiments in such a manner that healthy mice and mice inoculated by means of a tube *per os* were brought together in a way calculated to vary the concentration of the available infecting bacilli by altering the ratio of infected to non-infected animals. Two experiments, employing 100 mice each, were performed. In the first, when the proportion of inoculated to the uninoculated mice was 5:1, the mortality curve of contact mice agreed closely with that of the control curve based on the 20 mice each of which was given a fixed dose of the bacilli, whereas when the ratio was 1:1, the mortality of the contact mice was virtually negligible. In the second experiment, it was demonstrated that crowding increased the mortality. From the results of the several investigations and after comparing the resultant curves with the standard curve, the author concludes that his results "indicate that, with a given susceptible mouse population and a certain strain of mouse typhoid bacilli, the sporadic and epidemic prevalences of mouse typhoid are determined by the special and quantititave distribution of the bacilli. Under circumstances in which the entire mouse population is so exposed as to be in direct contact with an infecting dose of the mouse typhoid bacillus, the nature of the resulting mortality curve

depends upon the quality of susceptibility of the individuals composing the population."

**Comparative Study of the Kahn and the Wassermann Reactions for Syphilis.**—IDE and SMITH (*Arch. Dermat. and Syph.*, 1922, **6**, 770) presented a preliminary report on parallel tests in an unselected series of 2165 serums, using the precipitation reaction, as described by Kahn, and the Wassermann reaction, employing sheep cells and guinea-pig complement. Two antigens were used in each case, an absolute alcohol extract of human heart muscle, reinforced with 0.4 per cent cholesterin and an acetone and lipoid extract, with cholesterin as proposed by Kolmer. The fixation period varied from fifteen to eighteen hours in the ice-box. Of the 2165 serums, the results of the two tests were identical when more than two plus positives were counted. The authors believe that the Kahn precipitation reaction is almost as valuable as the Wassermann reaction on blood serum but indicate that it is not as efficient on spinal fluids. They state that anticomplementary serums give no difficulty with the Kahn test, such serums being either positive or negative.

## HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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**Results of Active Immunization with Diphtheria Toxin-antitoxin in the Public Schools of New York City (Manhattan and Bronx).**—ZINGHER (*Reprint Series, Dept. of Health, New York City*, No. 100, July, 1922) states that the immunity response to the same mixture of toxin-antitoxin varies greatly in different groups of children. A preliminary stimulation of the tissue cells in Schick-positive children caused by repeated exposure to infection with the diphtheria bacillus seems to enable the cells to give a better response to injections of toxin-antitoxin than in other children whose cells have not been previously stimulated by such exposure. This is the case even though these exposures have been slight and have not been apparent in the form of a perceptible increase of antitoxin in the circulating blood. After a first series of toxin-antitoxin injections, the immunity response to the second series did not follow the same inverse ratio noted between the original susceptibility of the children in a school and the percentage of successfully immunized children in the same school. Three doses of toxin-antitoxin, each from 1 to 1.5 cc, injected at intervals of one

week, give much better immunity results than 2 doses of the same amount injected one week apart. A longer interval between the injections of toxin-antitoxin has the advantage in allowing the local reaction to disappear more completely before the next injection of toxin-antitoxin is given. There may also be a better antitoxin response when the injections are given two weeks apart. At least six months should be allowed to elapse after the injections of toxin-antitoxin before the Schick retest is made to determine accurately the development of an active immunity. A second series of two or three injections of toxin-antitoxin should be given to those who have not become immune after the first series. There are a few children who fail to develop immunity after toxin-antitoxin injections even when they are given several series of injections. In the schools reported, from 70 to 93 per cent of children were rendered immune after two series of toxin-antitoxin injections. There is practically no danger from anaphylaxis, either in repeating the injections of toxin-antitoxin or in giving toxin-antitoxin after a preliminary injection of antitoxin.

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**Toxin-antitoxin Immunization Against Diphtheria.**—PARK (*Jour. Am. Med. Assn.*, 1922, **79**, 1584) summarized the results of twenty-five years of experimental and practical investigation of the immunizing effect of toxin-antitoxin injections and the value of the Schick test as follows: Three injections, 1 cc each, of a suitable toxin-antitoxin mixture spaced one or two weeks apart, will cause about 85 per cent of susceptible children or older persons to develop sufficient antitoxin to give the negative Schick reaction and produce marked, if not absolute, protection against diphtheria. The development of the immunity is slow. An amount of antitoxin sufficient to prevent the positive Schick reaction develops in different children in from one to six months after the receiving of the injections. Antitoxin, as heretofore, must continue to be used to produce immediate immunity. The duration of the immunity in at least 90 per cent of the children is for more than six years and probably for the remainder of life. There seems to be no difference in this respect between these, and those who develop antitoxin naturally. Toxin-antitoxin injections should not be given within two weeks after an injection of antitoxin; otherwise the toxin is slightly overneutralized and the resulting development of antitoxin is lessened. Mixtures made from old toxin and antitoxin are fairly stable and may be used for a period of one year. Even such preparations are at their best when first sent out, as the mixtures slowly tend to become at first neutralized and then slightly antitoxic. This change gradually lessens the immunizing power of the toxin. The toxin-antitoxin should be kept cool and in a dark place; it is best to use the mixtures within three months after their final preparation. A toxin-antitoxin mixture of stabilized materials which is safe when it leaves the laboratory cannot become more toxic on being kept. No serious effects ever have resulted from the injections given to the tens of thousands of the New York children in the past seven years. The Schick test is an extremely reliable means of separating those individuals who have antitoxic immunity from those that have none. Although a simple test, it must be carried out with extreme care. The toxin must be retained intracutaneously, and the toxin

must be neither 25 per cent more nor less than the desired amount. It is extremely important to choose glass of suitable chemical composition for the containers in which the toxin is to be placed, as otherwise rapid deterioration may take place. The preliminary Schick test is usually omitted in children under three years of age. This is for two reasons: (1) Two-thirds of these children require the toxin-antitoxin injections anyway; (2) it is not certain whether those that do give the negative reaction are immune because of an unusual persistence of the antitoxin given them by their mothers, or because of the active development of antitoxin in their own bodies. After this age the test is desirable, but it is often omitted. Thus, in practical school work, the first Schick test is frequently omitted in children up to six years of age because it is easier to inject the children at once rather than to delay for the test. At this age the percentage of children requiring immunization is still high, and the annoyance from the injections is slight. The omission of the preliminary Schick test facilitates the introduction of the immunizing injections in the schools. Above the age of six years, the preliminary Schick test should be made whenever practicable. No child should be pronounced immune from diphtheria because of having received three immunizing injections of toxin-antitoxin. A negative Schick test is absolutely necessary before one can properly make such a statement or issue a certificate. The use of the control-protein test made with the heated toxin is advisable at all ages when a careful separation of the pseudonegative reaction from the combined positive reaction is important. As with the Schick test, it is frequently omitted because of local conditions. The older the child the more likely it is to be immune and to give a confusing protein reaction. In children under five years of age, the protein reaction seldom confuses the picture if the Schick tests are read as late as on the fourth day; between five and seven years of age, the control does not help greatly in more than 5 per cent. In older children and adults, not only does the control protein test help us to decide more correctly in about 10 per cent of doubtful reactions; but when it is marked it also indicates with some probability those persons who are likely to have the marked local and constitutional reactions from the toxin-antitoxin injections. The toxin-antitoxin injections are inadvisable before the age of six months. During this time most of the infants retain the antitoxin received from their mothers. Up to the age of three months, immunizing injections are usually ineffective as the infant tissues do not respond sufficiently during this period to the toxin-antitoxin to produce antitoxin. Under usual conditions, it is probably safe to wait until the infant is nine months old and then to give the injections at the first suitable occasion. During the first three years there is almost no annoyance from the injections. As the child grows older, the danger from diphtheria gradually lessens, and the percentage of those developing annoying local and constitutional reactions slowly increases. The immunization of school children in acting to prevent their contracting diphtheria also lessens the exposure to infection of the younger children of preschool-age in their families. There appears to be no difference in the degree of immunity between those individuals who have developed antitoxin from natural causes and those who did so because of the stimulus of the toxin-antitoxin

injections. Institutions in which the children have been given the immunizing injections have been remarkedly free from diphtheria. The school children who have been injected have had one-fourth as many cases as the untreated children, and these cases have been of less severity.

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**The Tetanus Bacillus as an Intestinal Saprophyte in Man.**—TENBROECK and BAUER (*Jour. Exper. Med.*, 1922, **36**, 3, 261) state that the only reliable method that can be used for the detection of tetanus bacilli is the culturing of the suspected material, the isolation of tetanus-like organisms and the demonstration that the pure cultures form a spasm-producing toxin that is neutralized by tetanus antitoxin. Using this method, the authors demonstrated tetanus bacilli in 34.7 per cent of stools from 78 individuals in Peking. The tetanus bacillus grows in the digestive tract, for it is present in individuals who have been on a practically sterile diet for a month or more, and one individual may eliminate several million spores of tetanus bacilli in a single stool.

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**The Relation of Physical Defects to Sickness.**—COLLINS (*Public Health Rep.*, 1922, **37**, 2183) studied records of physical examination and school attendance during the school session 1920–21 kept for 3786 children in four fairly representative localities in Missouri. These children were classified according to physical condition and the absences from sickness and from causes other than sickness were compared by age groups for children of different physical conditions. The author states that children with no defects were absent from school on account of sickness consistently less than those with defects. Children with enlarged or diseased tonsils were absent more than children with no defects, and those with enlarged or diseased adenoids or tonsils associated with other defects were absent considerably more than those with enlarged or diseased tonsils only. Decayed teeth showed little or no effect on absence, and defective vision failed to show a consistent effect on absence from school on account of sickness. Absence from causes other than sickness showed variations somewhat similar to absence from sickness; the groups with defects were absent more than the group with no defects.

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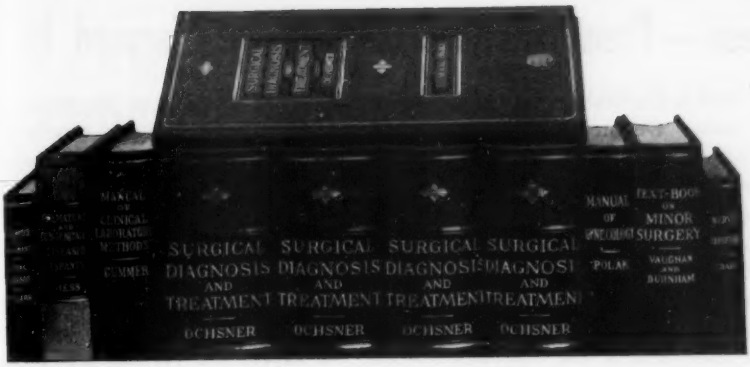
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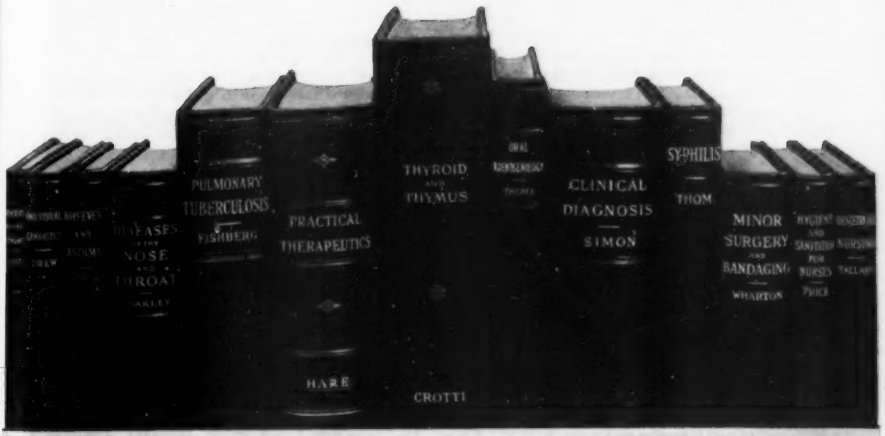


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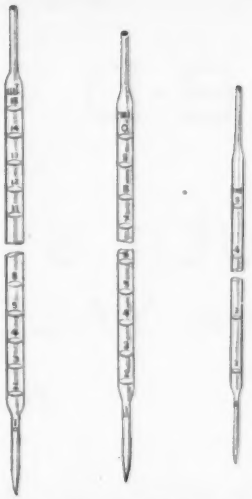

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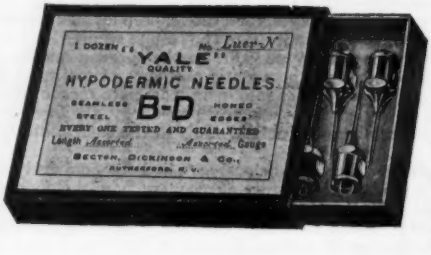


Yale quality needles represent more than 20 years of experience in manufacturing high grade needles.

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RUTHERFORD, N. J.

*Makers of Genuine Luer Syringes, Yale Quality Needles,* **B-D** *Thermometers, Ace Bandages, Asepto Syringes, Sphygmomanometers and Spinal Manometers*

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